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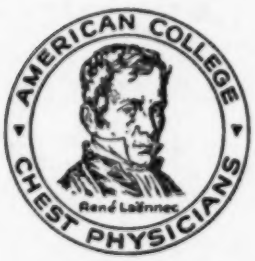
VOLUME XXVI NUMBER 4

# DISEASES

## *of the*

# CHEST

OFFICIAL PUBLICATION

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AMERICAN COLLEGE OF CHEST PHYSICIANS




EXECUTIVE OFFICE
112 East Chestnut Street, Chicago 11, Illinois
MURRAY KORNFELD, *Managing Editor*

VOLUME XXVI OCTOBER, 1954 NUMBER 4

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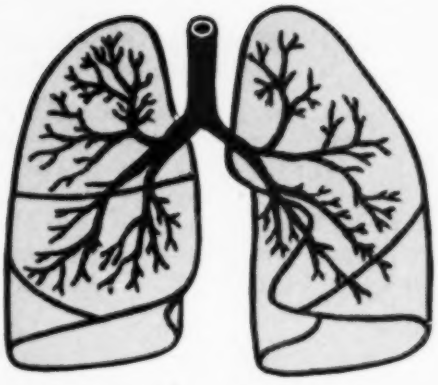

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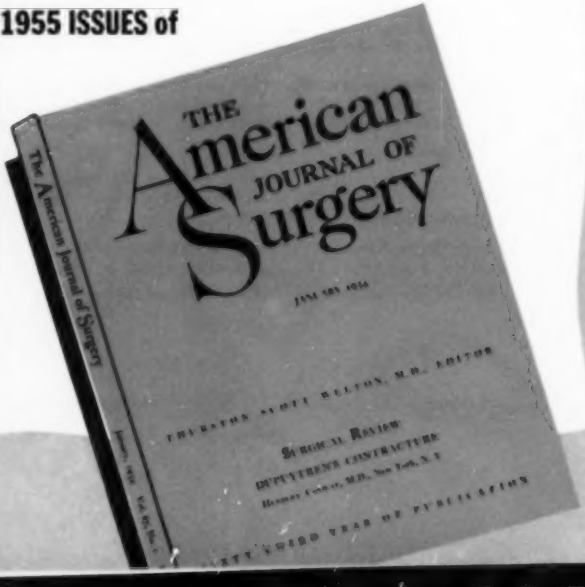


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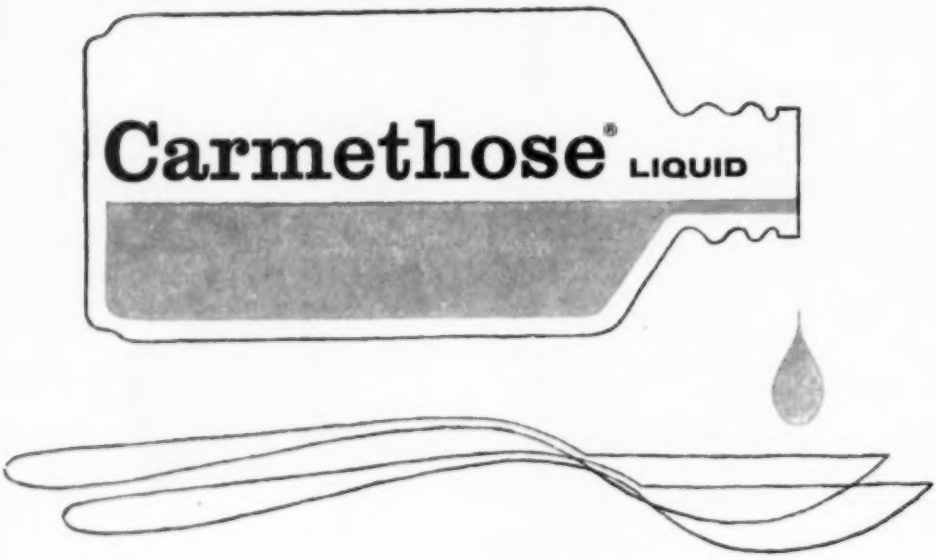


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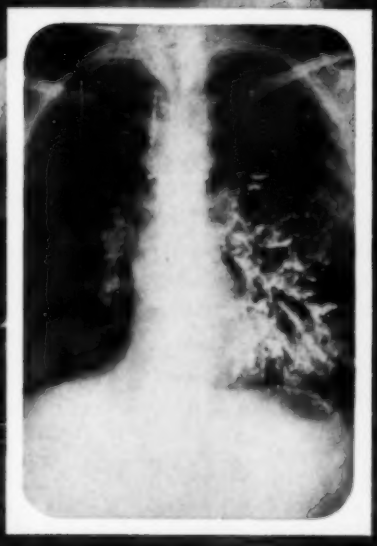

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DISEASES of the CHEST

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# Delirium Cordis*

**A heart-to-heart talk on certain problems in present day cardiology in the light of ancient and recent history.**

WILLIAM B. BEAN, M.D., F.C.C.P.
Iowa City, Iowa

Anyone with a reasonable mixture of pride and vanity in his makeup naturally takes it as a high honor to be asked to give the after-dinner sermon before such an illustrious company. But the honor carries the less happy implication that the speaker should combine wisdom and wit. Following in the wake of wise men and entertainers I have some qualms. The whole business assumes an aura of unreality. At this stage perhaps we can all get some consolation in blaming your speakers committee. At least it is too late to do anything about it now. One of the firmest planks in my platform of conviction and behavior is that physicians as members of an ancient profession owe society, or as I prefer to say, our fellow man, a debt of thoughtful criticism. If criticism is to have value it demands the use of the intellect. This enterprise few indulge in because it is such a wearisome and hard thing; and society has never had the full attention of the rational mind to help solve its problems. But in spite of their difficulty intellectual exercises may have a slight side all can enjoy.

From time to time the artist backs away from his canvas, changes the light and looks at his creation from a different and more distant place. He stops the act of embodying his percepts and concepts in the process of painting in order to get a general view of his progress. So as crafts-men in many fields of endeavor whose interesting collaborative venture is being recognized in this act of feast and assembly, let us stand back from our several parts of the scientific, social, and humanitarian mosaic to see whole the object of our joint work. Let us remove our thoughts from myopic concern with details, look up and regain in simplicity the sense of rejoining the world at large.

In giving my scattered remarks the formidable title of Delirium Cordis my purpose was to pose a question as well as to puzzle the thoughtful. You may note a recurrent theme of the dim view. I have prepared some

From the Department of Medicine of the College of Medicine of the State University of Iowa.

*This paper is derived from remarks made at the Annual Dinner of the Los Angeles County Heart Association, 20 October 1953 on the occasion of the 23rd Annual Symposium on Heart Disease, and at the Annual Banquet of the Iowa Heart Association and the Iowa Tuberculosis and Health Association in Des Moines, 14 April 1954.

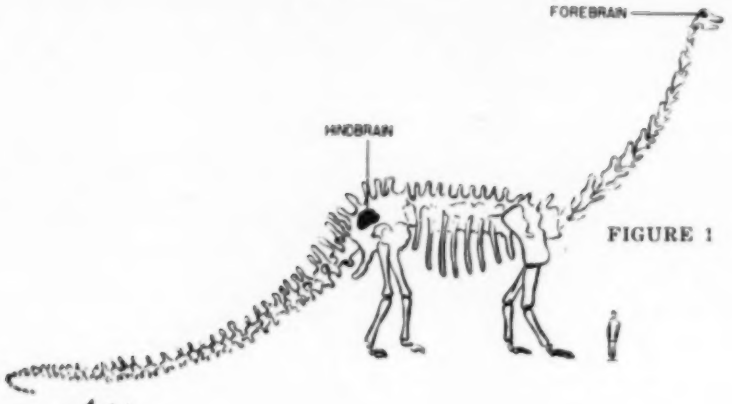


FIGURE 1

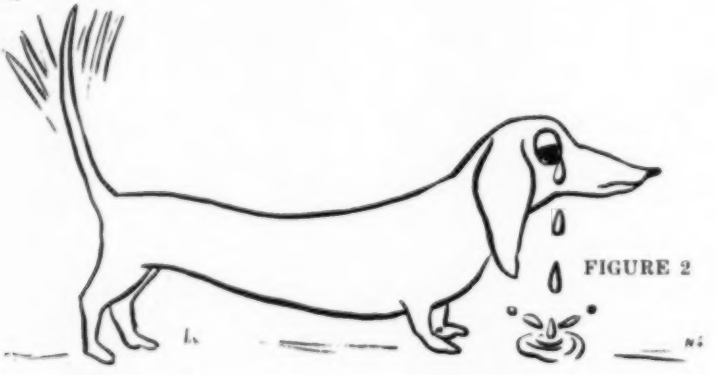

FIGURE 2

FIGURE 3

verse around a few borrowed lines to start us along in a mellow mood of perplexity. The whole talk, as you will see, is a series of non sequiturs presented in perfectly logical sequence.

Psychiatrists have made it plain
We have a fore and after brain
Which struggle for the upper hand
Reason or lust may take command
The dinosaur is now extinct
Because his two brains were distinct.

"You will observe by these remains (Figure 1)
The creature had two sets of brains
One in the head, the usual place
The other at his spinal base
Thus he could reason apriori
As well as a posteriori
No problem bothered him a bit
He made both head and tail of it
If something slipped his forward mind
'Twas rescued by the one behind
And if in error he was caught
He had a saving afterthought."
But sometimes two brains disagreed
The one said—loaf, the other—feed.
While forward brain would make him smile
His rear brain told him he felt vile—
Hind brain intent on procreation
His front brain favored sublimation.
At length the dinosaur decayed
Because the eggs were never layed.
Some bones remain, a dismal track—
Footprints in nature's cul-de-sac.

But now of creatures who survive (Figure 2)
In spite of troubles, still alive
The dachshunds clearly illustrate
How poorly nerves may integrate.
This tearful face displays no notion
Of happy wagging tail's emotion
And when dismay demotes his tail
His barking front gives happy hail.
So, tail twixt legs, with facial glee
The fore and aft do not agree.

The centipede has numerous feet (Figure 3)
The nerve supply of each so neat
That she can well perambulate
Both fast and slow, both curved and straight.
The centipede was very gay
Until a frog in fun did say
Which leg comes first, which next, which last?
What makes them slow, what makes them fast?
This raised her mind to such a pitch
She lay distracted in a ditch
Her quivering efforts came to naught
She could not walk by taking thought.
But when she gave up introspections
Her walk was brisk in all directions.
A moral is not hard to find.
Employ but do not fret your mind.

Such introductory masterpieces
Are only smoke screens for my thesis
Which is that we must all be led
*By heart* as well as brilliant head.

Now, let us leave the dry land of preparation, the shifting tides and currents of introduction, and come at length to the high seas of my sub-

ject. We may suppose that the voyage of man and his heart which we are taking had its beginning in the dim wastes of prehistory. It has continued during historic times with the records of our predecessors increasingly clear and more detailed into the present with the accumulations of research now piling up so rapidly that our understanding and thoughtful use of them still are largely matters for the future. Some few landfalls in this voyage I shall indicate.

Probably the cardiovascular system of man and its relation to his central nervous system, brain or mind, as we choose to say, has undergone no radical change during the most recent developmental phases in the span measured by late prehistoric and historic times. Paleopathology or study of the diseases in ancient times is well established. It indicates no basic changes in types of heart disease. It reaches back a mere instant in the long series of changes which have culminated in man as he is today. Unfortunately we have no paleophysiology. Perhaps the nearest we can come to it is to trace back in the archeology of language some concepts which are so firmly embedded in the matrix of man's linguistic heritage that we have reason to look upon them as natural objects of great significance.

To get further information concerning the attitude of man to his heart during ages for which we have no precise historic record, we approach it by speculation and imagination. It is reasonable to assume that the intimate connection between the activity of the heart and mental activity was perceived, perhaps dimly, by prehistoric man in remotest antiquity. This became of significance only when abstract thought advanced to the point where it permitted man to conceive of a separation between soul and body. Man placed the seat of the soul in the heart. This is reflected in concepts which we can trace most clearly in what we know and can infer about language. Even with the advance of scientific research which has demonstrated that the heart is really a muscular pump and insofar as we can get evidence, not the seat of the soul, the linguistic habits of our ancient forefathers prevail in their designation of the intimate relationship between heart and soul. I need not detain you with a great number. We know that Mrs. Smith has a heart of gold or a kind heart; Mrs. Jones has a heavy heart; that Mr. Thompson has a heart of steel or a heart of stone; that Tom is light-hearted; that Elizabeth is not a bad person at heart. When someone comes to me in a mood of confidence he opens his heart to me and I take his problem to heart. As I mentioned in the subtitle, we are now having a heart-to-heart talk. There are countless other expressions and only a few need be listed—soft-hearted, hard-hearted, heartless, broken-hearted, half-hearted, I win somebody's heart, I lose my heart to someone, I gain my heart's desire, something is heart-warming, heart-breaking. Hearts ache. Hearts are lonely. Folk speech invents a cardiac anatomy with heart cockles and heart strings. In the title of my comments the delirium or mania of the heart, though it is commonly used to designate a particular kind of irregularity or lack of rhythmic beat of the heart, illustrates as did the verse the fact that hearts may be mixed up and troubled. This symbolization of the heart remains as a pleasant

tribute to the persistence of folk speechways at a time when our understanding of its intricate functions has advanced in ways which are as remarkable as they were unexpected even the relatively few short years ago. Nonetheless, the heart stands squarely before us as the organ whose diseases and disordered workings are most likely to bring our career to an end.

Instead of taking you all on a detailed historic pilgrimage of heart disease I have chosen to spend a few moments in recalling to some, and introducing to most, one of cardiology's forgotten knights, Peter Mere Latham, whose career was at its peak in England about a hundred years ago. He was a man of charm and wisdom and simple piety whose example should be more widely known and valued today. His life I shall not detail. For several years I have been collecting some of the gems of his writings. A few I will pass along, realizing that such a concentration may lead to a surfeit and is better sampled one at a time. Most of these come from his text of cardiology. As he said of someone else "he could wrap up wisdom in a witticism."

## *Heart*

There is no organ of the body which during life submits its structural condition so freely to our knowledge as the Heart.

The Heart using its proper language of sounds and impulses, how clearly and emphatically does it speak of its own diseases to the ear and touch of experience.

Observation has traced back, with fearful fidelity, a long line of formidable and fatal diseases to their pathological parentage in the heart.

In speculating upon diseases and disorganizations of other parts as the causes conductive to disease and disorganizations of the heart, we must be cautious that we do not invert the real order of things. For the order of causation will be found to run as often from the heart to other organs as from other organs to the heart.

In every organ of the body, and pre-eminently in the heart, the living actions and sufferings of disease have a compass and a reach far beyond its material framework.

Only consider for a moment the proper office of the valves. They are meant (as it were) to keep guard at the orifices of the heart, and throw them wide open to the onward course of the blood, and hold them close-barred against its refluent current. But disease spoils their fitness sometimes for this office, and sometimes for that.

Valvular disease on the right side of the heart alone is a most rare occurrence; and, when it is found on both sides together, the disease on the left generally so far outruns that on the right, as to have reached its acme before the other has hardly begun.

Strange things happen to the heart when the chest is deformed.

Deformity of the chest, resulting from curvature of the spine is justly reckoned among the causes capable of producing disorganization of the heart, especially active or passive dilatation; or, it may be, dilatation both of one kind and the other coexisting in the several cavities of the same heart. The whole chest being distorted and narrowed, and the lungs straitened and imprisoned, and the heart itself displaced and the aorta tortuous, and the liver bearing hard with its external pressure, lead upon the whole to as large an amount of hurtful encroachment of organ upon organ as can possibly be conceived. And this encroachment cannot be without mechanical impediment; and this impediment cannot be without hurt and hindrance, first, to the functions, and then to the structure of such organs as the heart and lungs.

Because inflammation of the heart tends to a destructive disorganization, every day that it is allowed to abide and continue its progress, the heart sustains more and more injury from morbid matter deposited upon it or within it, and its functions are hindered and baffled, and at last abolished; and these functions are vital.

. . . One principal object I have in view is to bring diseases of the heart to a living test; to stand by the bed side, and there see how much we know of them, and how much we conjecture, and how, according to degrees of probability, our conjecture is made, sometimes little less than knowledge, and sometimes little more than a guess. Now we are able during life to conjecture a fat heart with such strength of probability that we almost know it.

By what agency does the heart become disorganized in consequence of a dilated aorta? It is, probably, by its own extraordinary efforts to overcome a virtual impediment to the circulation. Blood being immediately poured from it into a larger space than natural, requires from the heart an augmentation of its motive impulse.

Subjects of asthmatic diseases furnish the most frequent instances of dilatation of the heart from causes seated in the lungs.

What exact relation such disease of the kidneys bears to hypertrophy of the heart, we do not know even yet. But the two are too often coincident in the same subjects for them not to bear some, and that a very important, relation to each other.

The plainest and most palpable effects of an unsound heart upon the circulation in the veins are denoted by their distended and overloaded state . . .

Nature does, as it were, make use of the lungs as the readiest and the nearest channel through which to relieve the oppression of the heart.

It would be difficult to overrate the value, as guides to practice, of the signs which declare themselves through the medium of the lungs in every case of unsound heart.

What can be said of palpitations of the heart, and intermissions, and irregularities of its beats, which come and go during a man's whole existence, neither originating in any known disease, nor terminating in any, nor abridging in any measure the duration of life.

A little edema of the ankles . . . is the earliest beginning of serous effusion, which may go on increasing until it has pervaded the entire cellular structure and filled every serous cavity of the body.

There are no certain measures of pain, of palpitation, and irregular action, annexted to a given amount of unsoundness in the heart.

The heart that has a valve thickened and an orifice contracted, or its pericardium adherent, is apt to suffer pain, and to palpitate and beat out of time.

Learn, then, to read aright the meaning of these two orders of symptoms referable to the heart,—the vital and the mechanical.

I would state then summarily, that it belongs to the heart, in its different states of permanent unsoundness, sometimes to affect the brain perilously or fatally, the brain itself being altogether free from disease; and sometimes only to bring disease, which already exists within the brain, sooner, and more inevitably, to a perilous and fatal event. The work may be entirely of the heart, or it may be shared between the heart and the brain.

The man, who, having an unsound heart, must traffic with his sinews, for his daily bread, has a poor chance of benefit from medicine.

What a gain will it be to mankind, should observation hereafter discover that the conversion of the valves of the heart, and the lining of arteries, into earthy matter or cartilage, has its sure pathological origin in certain forms of disease in other parts, or in the constitution at large, which are both obvious and curable, or in certain habits and modes of living which can be rectified or avoided!

## *Heart Sounds and Murmurs*

The sounds which naturally accompany the movements of the healthy heart, can only be learnt by the practice of listening to them. It is useless to describe them.

*Murmurs* are to be caught quickly, and distinguished surely, and turned to a ready use, only by practice.

The ear must be a well-educated and well-practised ear, or it is not a trustworthy witness.

In proportion as the *sounds* of the healthy heart are more highly intonated, they acquire a greater audible extent. The louder they are, the further you hear them.

The abnormal murmurs, as well as the natural sounds, of the heart, are heard to a greater distance in proportion to their mere loudness, and that not only in the direction to which the current of the blood conducts them, but in all directions.

Thus the disease and the impediment still increasing may, and sometimes do, reach a point at which the endocardial murmur ceases thenceforth, and altogether, as long as life remains.

As to the *sounds* themselves, since the ear can only become familiar with them by practice, I leave you to be your own instructors. As to their theory, taking the matters of fact and matters of speculation which have been brought to bear upon it, I consider that it is in part satisfactorily made out, and in part only plausibly surmised.

If in a healthy man we carry bleeding far enough to blanch the surface of the body, we create an audible systolic murmur in the precordial region, and diffuse it through the arteries.

Place the instrument upon the neck by the side of the trachea, and pretty close to it, and at the same time rest your finger upon the space between the angle of the jaw and the mastoid process; and when your ear has caught a continuous humming sound, and listened for a while and made sure of it, then press your finger firmly down upon the vein, and the sound, if it be the true venous murmur, will immediately cease; then raise your finger, and if it be the true venous murmur, it will immediately return.

The truth is, a very free current of blood is essential to the production of the venous murmur.

Never omit to listen to the praecordial region whenever you visit a case of acute rheumatism, and visit a case of acute rheumatism oftener perhaps than you otherwise would do merely for the sake of so listening.

The short physiological account of auscultation, which has just been given, will probably be found useful to us as we proceed. At all events we may make a platform of it, where we think it will bear us, and tread more cautiously upon it, where we think it will not.

## *Pulse*

Surely the number of the *pulse* ought to have a vast deal to teach us, seeing what a point we make of ascertaining it in every instance. The pulling out of the watch, and the deliberation which follows, must appear to the patient at least the most solemn part of the interview with his physician.

The oracle of old made it the top of wisdom to know oneself, but did not fix the credit due to that fragment of self-knowledge which enables a man to keep count of his own pulse.

Now let us come face to face with the present. We are living in a time of crisis rarely equalled in human history. Behind the ironical fantasy of the so-called "peace" we have the sterner reality of iron curtain and cold war. Against the theme of the insistent roar of jet engines we witness vast world-wide disorder. The removal of the veneer of inhibitions of civilization reveals surprisingly near the surface the savage in man. Scratch the man of mid-century and find the Neanderthal. Intellect has not superseded instinct. It has only made the chances of response infinitely various. The absolutes which have governed professional standards of physicians and men of good will on their long pilgrimage have been eroded and sometimes ruined. The old certitudes, and sanctity of the individual, the authority of reason and knowledge, have been thrown out contemptuously to reveal the naked manifestations of power and evil. The cynic, protected by office, can apply the lynch law to character with

conviction automatic after mere accusation; and smoking out the rats burns down the house.

The all-enveloping mood of fear with its irrational tensions underscores man's frightening and tragic predicament. How can he get along with his fellow man—individually, nationally and internationally? To some extent a group like this exemplifies one of the healthy counter-currents which justifies our putting aside the bleak pessimism which dominates so much of our thought and action today. Medicine has been through other major ordeals when a general disintegration of the conserving and cohesive forces of the body politic loosened the ties of family and state. The connective tissue of society tends to dissolve. It sags, relapsing into barbarism, for the society and civilization we know are possible only through the active collaboration of the people and their willingness to subordinate private interest to common weal.

Although the ideals of medicine and its code of ethics have been high, its present esteem and public confidence is not a century old, and could easily be destroyed. We must prevent its succumbing to the disorder of our age, intellectual and spiritual paralysis with decay of moral standards, loss of professional cohesion and the narrow ultraspecialization and self-interest with the trade union spirit predominating. It is as true today as ever that the medical profession can exist and survive only as it is permitted to sustain its rights, privileges and prerogatives by popular confidence in integrity which must be self-monitored; and by public belief in its capacity for good. Medicine today suffers from a curious dichotomy which has vexed man in his dealings with the world from time immemorial. Some who profess themselves to be ultra scientific, search only for objective data in nature and make no effort to corral the meaning. On the other hand some philosophers and thinkers looking for ultimate meanings fail to get them into any coherent relationship to the objective data of science. Both have the illusion that they seek to find the truth but only with thoughtful combination of the two approaches is it possible to satisfy the intelligent layman's firm sense of reality and sense of the truth.

Let us now look at complexity from the point of view of the developments in cardiology which have flourished so furiously within the last few years that such a man as Latham might be completely at a loss to understand what the scientific jargon really meant. In spite of the fact that we do not have a completely filled-in story of the natural history of many diseases for example, high blood pressure or arteriosclerosis, the hard discipline of clinical observation is yielding results which are in a continuum of diminishing returns. It is unlikely that even very valuable information will revolutionalize our outlook and attitudes.

The great gifts of science have pushed aside the ravages and indeed the risk of infection so that more and more people are now permitted to die without the help of germs. In spite of what I observe here to be a strong effort on the part of automobile drivers to eliminate each other and pedestrians in a perpetual open season, from a statistical point of view this destructive force has not yet wiped out the gain from control of

infections. The pattern of heart diseases—the large increase in incidence of hardening of the arteries with its several potentially ruinous effects, and the prevalence of high blood pressure—shifted the focus of attention to those disorders which become commoner and more frequently disastrous in older people. There is even the danger that concentration on the ills and ails of the aged will bud off a new and independent specialty which will suffer by being cut off from the central core of medicine. The risk is especially bad if it follows the assumption that the elderly are not people at all, just as the false assumption that children were not people has been such a stumbling block to certain specialists in the field of pediatrics.

The radical and revolutionary new developments of cardiac surgery in a decade or slightly more have allowed the surgeon to invade that once inviolate sanctuary of the body, namely the heart, without pain, with surprisingly little danger and sometimes with results so magnificent that they fall almost in the class of fable. These gains are all based on a clearer understanding of function of the heart, circulation and breathing. They have been possible only because of a number of simultaneous but tangential developments in the fields of anesthesia, of nutrition, a knowledge of fluid and electrolytes, in the control of infections by antibiotics, and in the clearer diagnostic methods which were possible only with such newer techniques as cardiac catheterization, gas analysis and evaluations of cardiac function. To those working on the local scene, your contributions have been an inspiration and a means to achievement. As I see it, however, there are two hazards which are not negligible. The first is that cardiology becomes an independent specialty in its own right separated again from the main central current of the broad stream of general medicine. This hazard exists partly because research and specialization in our present scientific and medical structure are apt to come before the physician is tested in the crucible of learning the clinical arts. The eternal danger is that he becomes a superspecialist before he becomes a good doctor. This is a hazard of all specialization. It is a risk to be taken because of the enormously fruitful results which scientific specialization has made possible in numerous fields. Even to one who had his undergraduate training in medicine in the not too remote past, the complexity of recent developments is an increasingly difficult burden and I need only mention some that come to mind. The field of electrocardiography with its multiplication of leads has required a complete reorientation in the dynamic significance of what the electrocardiogram is able to tell us. Ballistocardiography is a totally new and perhaps important field. The recent exploitation of vectorcardiology presents another facet of interest. The complex findings of the cardiodynamic investigation with the intracardiac catheter has added to the complexity. All these and many others are being unrolled in splendid panorama by the participants in this symposium. It is a display of stunning virtuosity which leaves us recourse only to the virtue of humility. Now each of these functions has something to add to our understanding of the state of health or disease which is the lot of a particular individual. It needs to be added to a thorough and

firm grounding in clinical medicine with its knowledge, physical signs, interpretation of symptoms, or fluid and electrolyte physiology, of cardiodynamics, the field of therapeutics and the use of the x-ray film and the fluoroscope for extension of the physical examination. Good research technics bring useful additions to our information about basic mechanisms of circulation. In recent times we have seen coming into flower a relatively new investigator whose interest is mainly in the exploitation of a method or a gadget or a machine. His knowledge of the problems of health and disease is not wide. He has no compelling interest in finding the solution for a particular problem. He approaches investigation by playing the field. He hopes that by trying a test under many circumstances and working with innumerable people he will get some useful results. This is a baneful result of overspecialization not only in medicine but in scientific research generally.

When I am teaching undergraduate medical students or trying to evaluate the skill and capacity of an intern and resident I sometimes try to find how far he could go in solving a patient's problems if, for a time, the electric current were shut off. It is dispiriting to see the helplessness with which many confront very simple problems in medicine when they are suddenly told to walk without crutches. I do not imply that it is always possible to find out exactly what is wrong without sometimes many and often very elaborate tests. But where a diagnosis can be made by a simple history and physical examination it is a great pity that the patient spends several hundred dollars in useless laboratory studies which are not simply aimed to confirm or quantitate what is already available from the careful consideration of the patient.

The risks of overspecialization were satirized by Herodotus, Plutarch, Cato and Voltaire to mention a few. This quotation from Voltaire's Zadig is not without its lesson. Zadig, a prince of Babylon, had been wounded in defending the honor of the princess he was to marry. "Her wounds were slight, and she was soon well again. Zadig's hurt was more dangerous. A spear had hit him near the eye and made a deep wound. Semire asked nothing of the gods save that her lover should get well. Night and day her eyes were bathed in tears. She lived for the moment when Zadig should be able to delight in her tender looks once more. But an abscess formed on the wounded eye, and made the worst to be feared. The great doctor Hermes was sent for from Memphis, and he came to Babylon with a numerous retinue. He visited the sick man and said he would lose his eye. He even predicted the day and hour when this disastrous accident would happen. 'If it had been the right eye,' he said, 'I should have cured it, but wounds in the left eye are incurable.'

"All Babylon while bemoaning Zadig's fate, marvelled at Hermes' profound knowledge. Two days later the abscess burst of its own accord, and Zadig was completely cured. Hermes wrote a book in which he proved that Zadig should not have been cured. Zadig did not read the book. As soon as he could go out, he prepared to visit her who was the hope of his happiness in life."

The nonmedical part of this audience must not get the notion that these

generalizations are pure irony and iconoclasm. It seems to me that this collaboration illustrates one of the unique methods by which some of the difficulties can be avoided. I shall mention several and elaborate briefly on a few. In the first place, such a group as this, working as a regional voluntary health organization, can make money available for problems which can be approached suitably by the group at hand. Research can be directed either towards a peculiar or unusually prevalent form of heart disease, or because people on the local scene have the necessary skill to attack specific problems. It is much easier to determine this for Los Angeles in Los Angeles or Iowa in Iowa than it is in New York or Chicago. (2) The local voluntary health organizations by constructive contributions to public and individual welfare, especially such decentralized and regional groups as this, are a healthy, trend away from the concentration of power, money and decision in Federal government. (3) Your Heart Association is a fine example of the kind of contribution public spirited and idealistic citizens can make. It counteracts some of the evil effects of enthusiastic lay support of fads and such inadvertently disastrous preoccupations as antivivisection. Progress in research in medicine in England has been to some extent hampered by the difficulty of having experimental animals readily available for humane endeavors. Thus it comes as a shock to us in this country that a surgeon in England may operate on patients before he has operated on animals. (4) The intelligent support of research, even if it is clearly defined and narrowly aimed, may yield rich by-products of unexpected discovery. So often discoveries are made completely without blue print. The well-trained and perceptive investigator very rarely makes a discovery which he has predicted and reached along strictly logical lines. In other words, the happy and observed accident is likely to be the revolutionary turning point in our ideas.

But there are certain negative or bad features in the program. (1) the single disease approach to research. Those of us who are teaching medicine are frequently disturbed by the fact that more generally applicable grants are not given to support a man whose ideas might lead him first to work in the field of dermatology and then cardiology and then endocrinology and perhaps then in some specific organ system like the liver or central nervous system. It is true that this suggests a good deal of vacillation in our independent investigator but there is more concern about the fragmentation of interest into so many separate organizations which stress say tuberculosis, cancer, heart disease, diabetes and the like. For the present this is a sound approach. I hope the day comes when society will enlarge in wisdom and gain the sensible and mature view that investigation, broad in outline, careful in organization and independently run frequently will produce better results than that for which the aim and object are too narrowly specified. (2) Research supported by a well organized popularity contest and by Gallup polls of current interest, with false promise of quick answers, is evil and dishonest. It should be emphasized again and again that money cannot guarantee results. In the light of all the exciting discoveries of the past the average layman looks upon a scientist as some superior being who, given the opportunity, is

able to make long strides stepping from miracle to miracle in scientific seven league boots. Nothing could be further from the truth. Scientists, though some do not like to admit it, are people. They make mistakes. Their judgments are fallible. There is a very considerable and I think inevitable emotional connection of a scientist with his work. Much of our modest capital of basic research has been used up. It needs restoring. The best that we can hope is that those who distribute grants for research will assign them more wisely than we have any right to think they should. At this point I introduce another verse before I come to the conclusion. It simply exemplifies some of the Babel of tongues which vexes the student's memory without increasing his grasp of history, and follows my planned sequence of non sequiturs.

An eponymic lament in the form of a dirge.

Ewart, Corrigan, Roger
Live in eponyms today
Frantzel, Fisher, Grossmann, Hall
Marfan, Osler, one and all
Monkeberg, Valsalva, Quick
Libman, Sacks, van Gierke, Pick
Heberden, Ayerza, Fick
Tell us how our hearts are sick.
"Keith, Purkinje, His and Flack
Conduct our hearts impulsive track
Block aberrant beats which might
Apall Paul Wood or gall Paul White"
Quell arrhythmias which could
Forestall Paul White and mall Paul Wood.
When conduction acts in frenzy
We are guided by Mackenzie;
Asystolic fits and chokes
Immortalized by Adams—Stokes
To this eponymic jelly
Broadbent, Branham, Cardarelli
Traube, Hill, Duroziez
Heartless heart men, let us pray.

Eisenmenger and Fallot
Rule the cyanotic flow
Traube, Rotch, de Musset, Hill
Known for murmur or for thrill.
Graves, Sontoni, Ebstein, Hope
Worked without a fluoroscope
Kartagener, Warthin, Pins
Save us from our heartfelt sins
Still today the names go on
January, Harrison
Dexter, Kempner, Culbertson
Mauer, Eliasch and Burch
Do not leave us in the lurch
Harken, Keefer, Katz and King
To the heart men let us sing!

## *Conclusion*

The laymen in this audience little know their many helpful functions in supplementing the physician's efforts. He is usually called too late and can bring too little to be of complete usefulness. His patient is scared, threatened with pain, with loss of income as well as the cost of illness. Fear of economic disturbances delays treatment and restricts its scope. Few physicians can confine their practice to diseases they can cure with

virtuosity and finality. As doctors we live lives of incessant compromise. The practice of medicine is a selection from a sad series of second best choices. In his studies, his plans and aspirations of what might be done, the good physician looks to the laymen for help, moral and fiscal. On behalf of all the physicians whom your earnest collaboration has inspired and whom your thoughtful contributions have aided directly, I wish to thank you as laymen with my warmest thanks for the stimulus of your benefactions.

You have, by your corporate efforts and instinctive sense demonstrated the capacity to foster the sturdy advance of knowledge and welfare. It is an endeavor which is humane and good. But these constructive acts only emphasize the further duty to understand all the wide ramifications, the subtle as well as the evident implications of what we are about. For a just and wise combination of heart and head is our only hope of fulfillment among the snares and pits which beset us on all sides. I cannot give you a map or guide book. But perhaps it is well for us all to recognize that man is at a nodal point in his long journey, and that nodal point happens to be a jungle.

Many of the animals which we know have existed on earth have disappeared, generally because their rigid overspecialization prevented them from adapting to some unexpected and radical change in environment. Man, as a social organism, has survived and flourished because, in his often clumsy way, he has been able to adapt. But nature makes no allowance for illusions. Man is the first and only creature whose survival on the globe is to some extent within the reach of his own thoughtful manipulations. But weakness or uncertainty or stupidity does not get a second try in nature. Even a cheerful and optimistic person should ponder the question of whether man can escape the responsibility for thinking or abuse the results of his thinking and the less objective but no less real aspirations and yearnings of his spirit. For in recorded evolution the price of failure is extinction. And busy nature will turn her hands to other tasks.

*Acknowledgments*

The theme and rhyme scheme of the verses are borrowed, mainly from the rich and fertile source of folk songs in the oral tradition. Some of the part about the dinosaur appeared in some Chicago newspaper in the 30's, or so I am told by Professor Robert L. Ebel who gave me the lines included in quotation marks. The dirge was formed around four lines taken from a verse published in that unassailably anonymous column of the Peripatetic Correspondents in the Lancet. The Latham excerpts are from a substantial collection I have gathered together and edited. I hope to publish them in the early future. Many of them are derived from his textbook on Diseases of the Heart, the American edition of which was published in 1847. I am indebted to Mrs. Naomi Schedl and Miss Mary Arp of the Department of Medical Art for the illustrations.

# The Clinical Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Chronic Pulmonary Disease.*

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Impairment of pulmonary function in chronic lung disease is due to many factors, related basically to the amount of fibrosis, the degree of emphysema and the status of the bronchial tree. Much of the disability produced by these factors is a result of altered pulmonary physiology rather than the effects of organic disease itself.[1, 2, 3] The fibrosis and emphysema produce interference with pulmonary ventilation, faulty distribution of air in the lungs and ultimate oxygen unsaturation of the blood. Bronchial irritation, whether due to foreign body, infection, or abnormal secretions will produce increased breathing resistance through bronchospasm, narrowing of the airways and retention of secretions. The thickened, edematous and spastic bronchiolar mucosa plays a big part in producing unequal alveolar aeration and perfusion and constitutes a reversible factor in the production of disability. Measures for the relief of bronchospasm and evacuation of retained secretions have, therefore, been effective in improving pulmonary function. Barach, Segal, and others[4, 5, 6] have amply shown the usefulness of aerosol therapy in this respect. Administration of aerosols generally depends upon the inspiratory effort of the patient to carry the vapor into the lungs. Frequently, however, adequate dissemination of the aerosol is prevented by physical limitations imposed by the fibrosis, emphysema and impaired diaphragmatic motion. To counteract the pathological alterations produced by these factors, Motley and his associates[7, 8, 9, 10] have developed the use of intermittent positive pressure breathing combined with simultaneous nebulization of bronchodilator agents, antibiotics and other suitable drugs. Since intermittent positive pressure breathing increases both the minute volume of ventilation and the respiratory excursions, it was apparent that the aerosolized vapor would be more uniformly and more effectively distributed throughout the lung with better relief of bronchospasm and promotion of bronchial drainage. The present report deals with our experience over the past four years with this form of therapy in chronic pulmonary disease.

## *Method of Study*

The patients in this study consist of a group of 450 hard and soft coal

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Dr. Hurley L. Motley, formerly Director, Cardio-Respiratory Laboratory, carried out the physiological studies in most of the patients.

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miners with varying degrees of anthracosilicosis and pulmonary function impairment admitted to the hospital for detailed physiological study and a group of 300 patients with chronic pulmonary disease of varying types and degrees seen in clinics and in private practice. Selection of cases for treatment was based only on the presence of a significant degree of lung function impairment and the elimination of conditions which contraindicated this form of therapy, such as active tuberculosis, spontaneous pneumothorax and certain types of cardiac disease.

In each case a detailed history and physical examination was done. Routine laboratory studies in the hospitalized cases consisted of a complete blood count, urinalysis, blood sedimentation rate, fasting blood sugar, urea nitrogen, serologic test for syphilis, plasma proteins, tuberculin test and examination of the sputum as to volume, appearance, and the presence of acid-fast bacilli (plain smears, concentrates, cultures). Where no sputum was present, examination of the fasting gastric contents was carried out. Each patient was fluoroscoped and variations in the diaphragmatic excursions noted. Roentgenograms were obtained in deep inspiration and full expiration in the conventional posterior-anterior and lateral

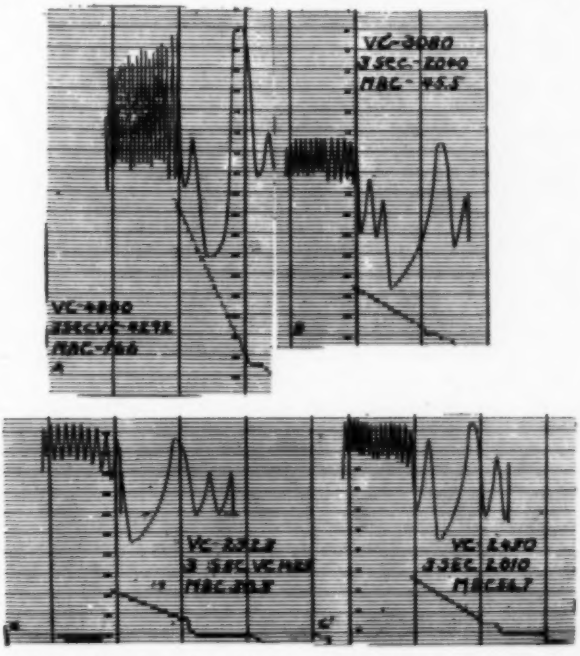


FIGURE 1: (*A*)—Spirogram of a patient with a normal vital capacity and maximal breathing capacity (medical student). (*B*)—Spirogram of a patient with a moderate degree of pulmonary emphysema. Note the abnormal shape of the expiratory curve. Nine seconds were required for complete exhalation. Although the total vital capacity was 3080 cc, the maximal usable part (3 seconds) was 2040 cc. (*C*)—Spirogram of a patient with third stage anthracosilicosis and marked emphysema before and after ($C^1$) eight days of treatment. Note the more effective expiratory curve after treatment with increase in the three seconds vital capacity.

projections. Other studies such as bronchoscopy, electrocardiograms, circulation times, iodized oil studies and planigrams were done as indicated. In a considerable number of the coal miners complete study of their pulmonary physiology was done.

Vital capacity and maximal breathing capacity were determined with a modified Benedict-Roth metabolism apparatus[8] designed to reduce the air resistance to rapid deep breathing by means of a large bell and large tubing. Multiple measurements were obtained in every case with varying rates and depths of breathing, and the values used were the highest obtained. Determination of the maximal breathing capacity was done with 12 second runs. The amplitude and rate of breathing and the total volume were recorded by two writing pens on an electrically driven kymograph. A permanent graphic tracing (spirogram) was thus obtained.

In 220 cases, vital capacity and maximal breathing capacity determination were made before treatment, after one treatment, and after a course of treatment with intermittent positive pressure breathing combined with a potent bronchodilator. A course of treatment generally consisted of three or four 20 minute applications daily for three to six weeks in the coal miner group and for 10 days to two weeks in the non-silicotic group. Longer periods of treatment were given in the more seriously disabled cases. The effect of therapy was evaluated by means of the degree of symptomatic and subjective improvement experienced by the patient, and objectively by repeated physical examinations, spirometric tracings, and roentgenograms. Improvement was recorded as none, slight, moderate, and marked.

Some patients were treated with the M.S.A. Pneophore and others with the Bennett Pressure Therapy Unit. In each case 100 per cent oxygen was used. The following bronchodilators were used with little variation in effect: isopropylarterenol hydrochloride (isuprel®, 1:200 dilution), racemic epinephrine hydrochloride solution (vaponefrin®, and cyclopentamine and isopropylarterenol compound (aerolone compound®). Eight drops of the bronchodilator were diluted with eight drops of normal saline or distilled water and the nebulizer adjusted until a fine spray was visible. The treatments were given with the patients in a sitting position and either a face mask or mouth piece and nose clip was used depending on the wishes and comfort of the patient. The control line pressure was generally set at 20 centimeters of water pressure. In some cases it was found desirable to set the pressure at a lower reading, particularly where there was a history of previous spontaneous pneumothorax or where the patient experienced some discomfort. The patient was instructed to inhale slowly and deeply (eight to 12 respirations per minute) continuing to breathe in until the lungs were full and to exhale completely. This was easily done with the flow sensitive apparatus (Bennett) which followed the patients' own breathing pattern. Patients with rapid, irregular breathing, such as occurred in advanced disability or in severe asthma, found difficulty with the automatic cycling pressure sensitive apparatus (Pneophore). If cough or expectoration were desired the patient was instructed to remove the mask or mouth piece temporarily.

The nebulizer was adjusted to deliver all of the medication within the period of each treatment. When maximum benefit was evidenced from the initial course of treatment, the number of daily treatments was gradually reduced and the patient transferred to out-patient ambulatory care.

### *Results of Study*

The type of cases treated is shown in table 1. All were males except 18. The majority were coal miners (64.5 per cent), 89 per cent of these having worked in anthracite mines and 11 per cent in bituminous mines. Hypertrophic emphysema, with or without associated fibrosis, was next in frequency and accounted for 19.7 per cent. Silicosis from exposure other than in coal mines, occurred in 6 per cent. The cases with tuberculosis were those in which the tuberculosis was healed and symptoms were due to the associated emphysema or bronchiectasis. The age for the entire group studied varied from 19 to 79 years, the average being 54.7 years. The younger ages were generally seen in those with non-silicotic conditions. The frequency and length of treatment varied with the condition but was generally more prolonged in the coal miner group who were hospitalized through the Anthracite Health and Welfare Fund. Prolonged hospitalization of the other groups was limited by financial con-

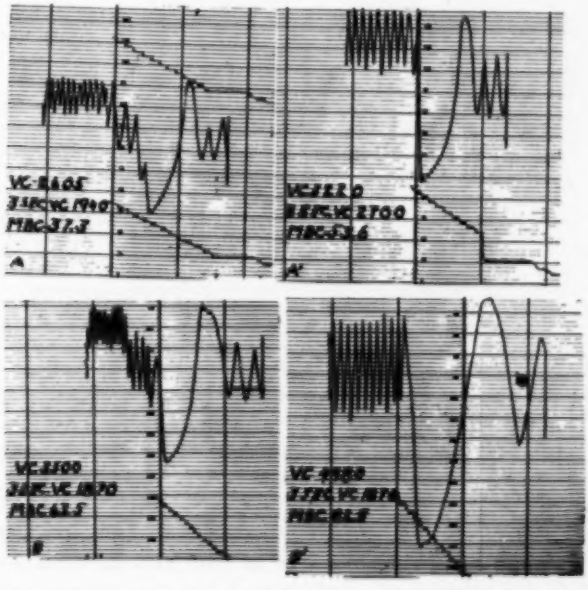

FIGURE 2: (*A*)—Spirogram of a hard coal miner with third stage anthrocosilicosis and marked emphysema before and after ($A^1$) a twenty minute period of intermittent positive pressure breathing with a potent bronchodilator. Note the increase in both vital capacity and maximal breathing capacity indicating the presence of bronchospasm. (*B*)—Spirogram of a soft coal miner with moderate anthracosilicosis and emphysema before and after ($B^1$) eleven days of treatment. The effective three second vital capacity has not changed although the total vital capacity and maximal breathing capacity have increased.

siderations. The figures as to number and period of treatments relate only to hospitalized cases. A considerable number of non-miner patients were treated on an ambulatory basis, the average treatment being one a day over a period of 35 days. In some cases treatment has been given on this basis over a period of three years.

TABLE I: TYPE OF CASES IN WHICH INTERMITTENT POSITIVE PRESSURE BREATHING WAS APPLIED

| Disease | Number of Patients |
|---|---|
| Anthracosilicosis | 483 |
| Emphysema | 88 |
| Pulmonary fibrosis and emphysema | 60 |
| Silicosis | 45 |
| Bronchiectasis | 27 |
| Chronic bronchitis | 15 |
| Bronchial asthma | 11 |
| Chronic pulmonary tuberculosis with emphysema or bronchiectasis | 7 |
| Asbestosis | 5 |
| Chronic lung abscess | 2 |
| Other conditions | 7 |
| TOTAL | 750 |
| Average age | 54.7 years |
| Average number of treatments | |
| Coal miners | 75 |
| Others | 33 |
| Average period of treatment | |
| Coal miners | 21.6 days |
| Others | 10.8 days |

The results of treatment from a clinical standpoint are summarized in table II. Evaluation was based on the degree of symptomatic relief gotten, the changes on physical examination and the fluoroscopic and roentgenographic appearance. About 19 per cent showed slight or no improvement and 81 per cent a significant degree of improvement. Greatest relief was experienced in those cases where bronchospasm and retained secretion were major factors. Improvement was manifested symptomatically by relief of dyspnea, with "lighter" and "easier" breathing, lessened cough and easier expectoration, and less tightness of the chest. Initially an increase in the amount of sputum was noted consistent with the promotion of bronchial drainage but ultimately a decrease occurred. On physical examination, a decrease in number or disappearance of musical rales was generally found after treatment. Little change was noted on the roentgenogram but better aeration on fluoroscopic observation was frequently observed. Many of the patients were able to increase their

activities after treatment and resume their daily routine with considerable less discomfort. In some cases return to work was possible.

Table III shows the average physiological measurements in 220 cases before and after treatment. Of these cases, 150 were coal miners. In about 15 per cent of all patients no change or a decrease in the figures for vital capacity and maximal breathing capacity was noted. In general, however, there was a significant increase in both measurements after one treatment and after a course of treatment, the increase being greater in the maximal breathing capacity. An increase in maximal breathing capacity generally indicated the presence of bronchospasm. In some cases no improvement was noted in the ventilation measurements but the patient reported considerable symptomatic relief after treatment. It is difficult to explain this discrepancy, but factors such as the influence of weather changes, the lack of equal effort by the patient each time, and normal variations in values must be considered.[11]

TABLE II: CLINICAL RESPONSE TO TREATMENT BY INTERMITTENT POSITIVE PRESSURE BREATHING IN 750 CASES

| Disease | Number Treated | Degree of Improvement: None No. | None % | Slight No. | Slight % | Moderate No. | Moderate % | Marked No. | Marked % |
|---|---|---|---|---|---|---|---|---|---|
| Anthracosilicosis | 483 | 25 | 5.2 | 62 | 12.7 | 248 | 51.3 | 148 | 30.8 |
| Emphysema | 88 | 6 | 6.8 | 10 | 11.4 | 34 | 38.6 | 38 | 43.2 |
| Pulmonary fibrosis and emphysema | 60 | 4 | 6.8 | 12 | 20.0 | 22 | 36.6 | 22 | 36.6 |
| Silicosis | 45 | 1 | 2.2 | 8 | 17.5 | 20 | 44.5 | 16 | 35.8 |
| Bronchiectasis | 27 | .... | .... | .... | .... | 15 | 55.5 | 12 | 44.5 |
| Chronic bronchitis | 15 | 1 | 6.7 | 6 | 40.0 | 7 | 46.6 | 1 | 6.7 |
| Bronchial asthma | 11 | .... | .... | 1 | 9.1 | 4 | 36.4 | 6 | 54.5 |
| Pulm. tuberculosis with emphysema or bronchiectasis | 7 | 1 | 14.2 | 1 | 14.2 | 3 | 42.8 | 2 | 28.8 |
| Asbestosis | 5 | .... | .... | 1 | 20.0 | 1 | 20.0 | 3 | 60.0 |
| Chronic lung abscess | 2 | .... | .... | 1 | 50.0 | .... | .... | 1 | 50.0 |
| Other conditions | 7 | .... | .... | 2 | 28.5 | 2 | 28.5 | 3 | 43.0 |
| TOTALS | 750 | 38 | 5.1 | 104 | 13.8 | 356 | 47.5 | 252 | 33.6 |

TABLE III: AVERAGE VENTILATORY MEASUREMENTS IN 220 CASES TREATED BY INTERMITTENT POSITIVE PRESSURE BREATHING

| | Vital Capacity (cubic centimeters) | Change (per cent) | Maximal Breathing Capacity (Liters per minute) | Change (per cent) |
|---|---|---|---|---|
| Before treatment | 2822 | | 59.2 | |
| After one treatment | 3020 | + 7.0 | 68.6 | +15.8 |
| After course of treatment | 3247 | +14.9 | 76.1 | +28.5 |

In table IV are recorded the responses in 483 cases of anthracosilicosis. All degrees of disease were present, but the coalescent nodular and conglomerate phases of the third stage accounted for about 67 per cent of the cases. A marked degree of associated emphysema was present in 47 per cent of cases and a significant degree of pulmonary function impairment in about 60 per cent. This was not surprising as 85.3 per cent of the miners had already stopped work due to dyspnea and other evidences of pulmonary disability. Improvement was striking in about 80 per cent of cases, particularly in those with marked disability. Relief was evidenced by "freer" and "lighter" breathing and the ability to get around easier. This was preceded in many cases by marked expectoration of thick, tenacious, black sputum for the first three or four days of treatment. Practically all patients gained weight and felt stronger. A decrease in the number and character of rales was noted but no significant changes on the roentgenograms was observed. In general, improvement lasted for about three months following a course of treatment, although

TABLE IV: RESULTS OF TREATMENT IN 483 CASES OF ANTHRACOSILICOSIS TREATED BY INTERMITTENT POSITIVE PRESSURE BREATHING

| Stage | Number | Degree of Improvement | | | |
|---|---|---|---|---|---|
| | | None | Slight | Moderate | Marked |
| None or borderline | 35 | 3 | 3 | 19 | 10 |
| First | 43 | 0 | 6 | 24 | 13 |
| Second | 85 | 10 | 8 | 44 | 23 |
| Third | 320 | 12 | 45 | 157 | 106 |
| TOTALS | 483 | 25 (5%) | 62 (13%) | 244 (51%) | 152 (31%) |
| Degree of emphysema | | | | | |
| None or slight | 90 | 4 | 12 | 51 | 23 |
| Moderate | 165 | 5 | 27 | 85 | 48 |
| Marked | 228 | 10 | 27 | 111 | 80 |
| TOTALS | 483 | 19 (4%) | 66 (13%) | 247 (51%) | 151 (22%) |
| Degree of function impairment | | | | | |
| None or slight | 34 | 2 | 14 | 14 | 4 |
| Moderate | 158 | 8 | 16 | 91 | 43 |
| Marked | 291 | 16 | 34 | 147 | 94 |
| TOTALS | 483 | 26 (5%) | 64 (13%) | 252 (52%) | 141 (30%) |

MEASUREMENTS (150 CASES)

| | Vital Capacity cc | Change | Maximal Breathing Capacity L/m | Change |
|---|---|---|---|---|
| Before treatment | 2941 | | 60.4 | |
| After one treatment | 3149 | + 7.1 | 70.5 | +16.7 |
| After course of treatment | 3246 | +10.4 | 83.7 | +38.6 |

it was longer for some and shorter for others. Some miners required daily treatment for a month or two before improvement was noted. Ventilation measurements showed rather slight improvement in the vital capacity after treatment but a more marked response in the maximal breathing capacity. This was not surprising in view of the marked degree of emphysema and disability present in this group.

Eighty-eight patients with so called idiopathic or hypertrophic emphysema were treated. The degree of emphysema was marked or very marked in 78 per cent and over one-half showed evidences of bronchospasm manifested by the presence of musical rales. Ninety-three per cent of these patients were noted to improve, over 80 per cent to a significant degree. The degree of improvement was especially gratifying in the advanced cases and was most marked where bronchospasm was present. The ventilation measurements showed more or less the same changes as in the coal miner group, undoubtedly due to the fact that a considerable number also had an advanced degree of emphysema.

The response to treatment in 60 patients with pulmonary fibrosis and emphysema was encouraging. In some the emphysema predominated, in others the fibrosis. In both groups, however, a significant degree of relief was obtained in 72 per cent. In five instances the degree of fibrosis was severe producing total disability. All of these patients have died but some measure of relief was given for awhile and life undoubtedly prolonged. The ventilation measurements indicate poor response to treatment but this is due to the influence of the five patients who have died. In the remaining 12 some improvement was noted similar to the response in cases of ordinary emphysema.

Twenty-seven patients with proved bronchiectasis were treated. All received a considerable degree of improvement manifested by easier cough and expectoration and a decrease in number of basal moist rales. The amount of sputum raised was initially increased but later was decreased. Occasionally slight hemoptysis was noted but this could not be attributed to the treatment. The number and severity of "chest colds" was definitely decreased in the treated group.

Poor response to treatment was generally noted in those patients considered to have non-specific chronic bronchitis unassociated with bronchospasm and retained secretions. The chief complaint in this group was chronic, non-productive cough. About half of the 15 patients with this diagnosis reported slight or no relief.

Patients under treatment with bronchial asthma showed immediate and marked relief, especially when wheezing was present. Less than 10 per cent reported only slight improvement. Improvement was manifested by decrease in wheezing, lessened cough and easier expectoration. Relief was not as pronounced in those cases where associated emphysema was present or where the allergy was related to endogenous factors.

In seven cases cautious application of therapy was made to patients with chronic inactive pulmonary tuberculosis in whom a significant degree of compensatory emphysema or postfibrotic bronchiectasis had developed. All of them were greatly disabled from the complication rather than from

the tuberculosis itself which in each case was considered to be healed. It was felt that bronchospasm, retention of secretions and impaired aeration were basic causes for aggravation of disability similar to that which occurs in persons with silicosis.[12] Intermittent positive pressure breathing produced a significant degree of improvement in five of the seven cases, attributed to increased bronchial drainage and better alveolar aeration. In three acid-fast bacilli were demonstrated in the sputa after several weeks of treatment. Whether this was a result of the dynamic treatment or whether the increased "washing out" of the bronchi made manifest bacilli trapped in the retained secretions is difficult to say. It was not felt that the treatment activated the supposedly healed disease, either from the increased pressure or from the use of 100 per cent oxygen, despite the work of Rich and Follis which indicated that the growth of tubercle bacilli experimentally was influenced by increased oxygen tension.[13]

In five cases of asbestosis dramatic relief was evidenced in three instances. These patients were hospitalized with marked dyspnea and examination revealed the presence of diffuse bubbling rales throughout both lungs. The clinical picture strongly suggested an increased pressure in the pulmonary circulation with right heart failure. Immediate relief of dyspnea with disappearance of the rales occurred after a few days of treatment. The improvement has been maintained by prolonged treatment on an ambulatory basis.

*Discussion*

Intermittent positive pressure breathing consists of active inflation of the lungs under positive pressure during inspiration and passive deflation during expiration produced mainly by the elastic recoil of the lungs and chest wall. This type of breathing differs from expiratory positive pressure in which the patient exhales against a positive pressure and from continuous positive pressure breathing in which the positive pressure is maintained during both phases of respiration. In intermittent positive pressure breathing the peak mask pressure varies with the line pressure which is adjustable from 0 to 30 centimeters of water. When the peak mask pressure is reached (usually set at 20), cycling of the valve occurs and expiration takes place at or about atmospheric pressure. The cycling valve may be pressure sensitive (automatic) or flow sensitive, responding to the patient's own breathing pattern in the latter instance.

Previous studies[14, 15, 16] have shown that intermittent positive pressure breathing does not significantly alter cardiac hemodynamics. The cardiac output is usually slightly decreased, but this reduction is less than that which normally occurs in man when changing from the supine to the standing position. The blood pressure in the systemic arteries, right ventricle and pulmonary arteries is slightly decreased, and a moderate degree of hyperventilation produced (6-10 liters per minute), but lowering the arterial p $CO_2$ can be controlled.[17] It will not produce distension of the lungs even with prolonged application and will not aggravate pre-

existing emphysema.[8] The maximum peak inspiratory pressure is never set at a pressure greater than 20 centimeters of water, a much lower pressure than that which occurs in an ordinary cough where the maximum pulmonary pressure varies from 40 to 100 centimeters of water. The pressure is also released during expiration and this phase occurs at or about atmospheric pressure.

Intermittent positive pressure breathing as used in this investigation manifests its benefits through five basic actions:

1. It provides more adequate ventilation of the lungs through increased minute volume and depth of respiration with no increase in the breathing effort. This was readily observed on direct fluoroscopy during treatment, especially where marked limitation of diaphragmatic motion was present. The bases of the lungs showed increased aeration with better and more efficient motion of the diaphragms. The increase in minute volume facilitates the "blowing off" of carbon dioxide and prevents the development of respiratory acidosis.[18]

2. It improves bronchial drainage. This is promoted during the expiratory phase by the high velocity expiratory gas flow produced by the rapid release of inspiratory pressure. The inspiratory flow rate is approximately one-half that during the initial phase of expiration. The rapidly falling expiratory pressure promotes the movement of sputum from the bronchial tree by a "sucking" action produced by the high expiratory flow rate. However, Barach[19] believes that bronchial drainage is mainly produced by the better aeration of the alveoli providing the subsequent cough with air behind mucous plugs.

3. It provides a more effective means for the dissemination of aerosols into the poorly ventilated areas of the lungs with relief of bronchospasm and improvement of bronchial drainage. Previous methods of aerosol therapy have depended largely on the patients' own inspiratory effort but the fibrosis, emphysema and poor motion of the diaphragm frequently associated with chronic pulmonary diseases has generally limited its effectiveness. Relief of bronchospasm can readily be demonstrated by the disappearance of musical rales and the improvement of ventilation measurements as shown in table 3.

4. It provides a more uniform and better alveolar aeration in all portions of the lungs. This improves the respiratory blood-gas exchange and results in an increase in the arterial oxygen saturation.[9] In many chronic pulmonary conditions, ventilation of the alveoli is generally impaired by mechanical obstruction due to fibrosis, loss of elasticity, bronchospasm, mucous plugging and retention of secretions. This in turn results in an increased oxygen transfer gradient (between the alveolus and the arterial blood) with a decrease in the arterial $pO_2$ and oxygen saturation. Intermittent positive pressure breathing lowers this transfer gradient by providing a more uniform alveolar aeration, especially of those alveoli which are poorly ventilated on ambient breathing but are still perfused with blood.[20] It does not improve the oxygen transfer in normally ventilated alveoli and has no effect on alveoli still perfused with blood but not ventilated due to complete blockage of the bronchiole. It also has no effect on

alveoli which are ventilated but not perfused. The beneficial effect of intermittent positive pressure breathing on the transfer gradient, therefore, results from improved aeration of alveoli with normal perfusion but with partial bronchiolar obstruction.

5. It provides an effective form of deep breathing with increase in tone of the respiratory group of muscles. Poor breathing habits, especially of the shallow type with insufficient respiration may generally be corrected. It has been shown that moderate exercise on a treadmill produces deeper breathing in coal miners, similar to that produced by intermittent positive pressure breathing, with resulting improvement in the gas exchange through better lung aeration.[21] Patients with good diaphragmatic motion may take their own breathing exercise and improve muscle tone, but intermittent positive pressure breathing offers help to thise with impaired diaphragmatic motion who are unable to exercise by their own efforts.

The results of treatment can be evaluated subjectively and objectively. As shown in table 2 about 80 per cent of patients showed a significant degree of improvement. Symptomatic improvement was consistent with decrease in breathing resistance through relief of bronchospasm and promotion of bronchial drainage and was manifested clinically by improvement in dyspnea, cough, expectoration, appetite and strength. To overcome the influence of psychological factors in measuring the degree of improvement, certain objective observations can be used. The disappearance of rales reflects the relief of bronchospasm and the evacuation of retained secretions. Better aeration of the lungs is revealed by increased illumination of the lung fields and improved diaphragmatic motion. The use of spirographic tracings obtained with the special large metabolism apparatus offers an important means of recording the nature and degree of impairment and the benefits derived from therapy. The time element and shape of the spirogram are important. When more than three seconds are required to blow out most of the air from the lungs after a deep inspiration, impairment is indicated. This may be due to loss of elasticity or to obstruction or to both. The volume of air exhaled in the first three seconds represents the maximal effective portion of the vital capacity and is of more significance than the total value for the test. Patients with emphysema manifested this impairment by prolongation of expiration time producing an abnormal curve as shown in figure 1. The presence of bronchospasm can be measured by the increase in vital capacity and maximal breathing capacity after treatment with a bronchodilator, as shown in figure 2. The rate and depth of respiration can be varied and an optimal relationship obtained which will produce the highest values for the maximal breathing capacity. In general, a patient must breathe about 80 times per minute to record a normal maximal breathing capacity. Intermittent positive pressure breathing generally affords an increase in this breathing rate with an increase in the maximal breathing capacity. In this series the maximal breathing capacity showed an average increase of 9.4 liters per minute, or 15.8 per cent after one treatment, and 16.9 liters per minute, or 28.5 per cent, after a course of treatment.

Intermittent positive pressure breathing has its greatest effectiveness in the early stages of chronic pulmonary disease where spasm and edema of the terminal bronchioles and retention of secretions constitute reversible factors in the production of disability. The relief of spasm and improvement of drainage will tend to delay the development of irreversible damage. When fibrosis and emphysema develop with thinning and rupture of the alveolar walls and loss of elasticity, then intermittent positive pressure breathing can do little except to give temporary relief. In the absence of demonstrable bronchospasm and other correctible features—when the patient is functioning at top capacity—then intermittent positive pressure breathing will have very little immediate effect. With prolonged treatment, however, beneficial effects will ultimately be manifested through its influence on the respiratory blood-gas exchange. It is in no sense of the word a curative procedure, but the degree of symptomatic improvement is frequently striking. The effect of treatment is temporary, necessitating frequent and prolonged application. In many cases it has been recommended that the patient procure a suitable apparatus for use at home under supervision of his own physician. This has been especially true in advanced cases of fibrosis and emphysema where daily treatment for prolonged periods was required.

Contraindications to the use of this form of therapy are few. It should be avoided in active tuberculosis, recent hemoptysis, and spontaneous pneumothorax, and should be used with caution where myocardial ischemia is a factor. Where severe coronary artery disease is present, phenylephrine hydrochloride (neosynephrine® hydrochloride) or isotonic saline solution can be used in the nebulizer. Bronchodilator drugs should be chosen with care according to the condition of the patient. Vasopressor drugs should be administered with caution in the presence of hypertension, generalized arteriosclerosis and coronary heart disease. Isopropylarterenal hydrochloride (isuprel®) and aerolone compound may be used in these cases as the effects on the pulse and blood pressure are minimal. However, 100 per cent oxygen should be used with all of these bronchodilator drugs as it protects against the vasoconstrictor action.

## SUMMARY AND CONCLUSIONS

1. Impairment of pulmonary function in chronic pulmonary disease is related basically to the amount of fibrosis, the degree of emphysema, and the pressure of bronchospasm and retention of secretions. Some of these disturbances of function are reversible.

2. Intermittent positive pressure breathing combined with nebulization of bronchodilators and other aerosols is an effective method of treatment of chronic pulmonary conditions where respiratory difficulty or insufficiency due to these factors is present.

3. The results of treatment in 750 cases of chronic pulmonary disease are presented of whom 5.1 per cent showed no improvement, 13.8 per cent a slight degree, 47.5 per cent a moderate degree and 33.6 per cent a marked degree of improvement.

4. Symptomatic improvement was manifested by lessened dyspnea, decrease in cough and expectoration and increased strength.

5. The degree of improvement was recorded objectively by determination of vital capacity and maximal breathing capacity before and after treatment. The vital capacity showed an average increase of 7.0 per cent after one treatment and of 14.9 per cent after a course of treatment. The maximal breathing capacity showed an average increase of 15.8 per cent and 28.5 per cent respectively.

6. Intermittent positive pressure breathing provides relief and control of symptoms through better ventilation of the lungs, improvement of bronchial drainage, more uniform distribution of aerosol to all parts of the lung with relief of bronchospasm, more uniform alveolar aeration and improvement in muscle tone.

7. The beneficial effects of intermittent positive pressure breathing are most pronounced where bronchospasm, loss of lung elasticity, and retention of secretions constitute reversible factors in the production of disability.

8. The details of treatment and the contraindications are discussed.

RESUMEN Y CONCLUSIONES

1.—El daño a la función pulmonar en las enfermedades crónicas del pulmón, está en relación de manera básica al volumen de fibrosis, el—grado de enfisema, la presión del bronchospasmo y la retención de secreciones. Algunos de estos trastornos de la función, son reversibles.

2.—La respiración bajo presión positiva intermitente combinada—con la nebulización de broncodilatadores y otros aerosoles, constituye un método efectivo de tratamiento en las condiciones crónicas cuando la dificultad respiratoria o la insuficiencia debidaaestos factores estápresente.

3.—Se presenta el resultado del tratamiento de 750 casos de enfermedades pulmonares de los que 5.1 no mostraron mejoría, 13.8 por ciento tuvieron ligera mejoría, 47.5 una moderada mejoría, y 33.8 una marcada mejoría.

4.—La mejoría se manifestó por disminución de la disnea, disminución de la capacidad vital antes y después del tratamiento. La capacidad vital mostró un aumento medio de 7.0 por ciento después de un tratamiento y 14.9 por ciento después de una series de tratamientos. La capacidad respiratoria máxima mostró un aumento medio de 15.8 por ciento y 28.5 por ciento respectivamente.

6.—El método de la respiración a presión positiva intermitente,-proporciona alivio y control de los síntomas por la mejor ventilación-de los los pulmones, mejoría de la canalización bronquial, más uniforme distribución del aerosol a todas las partes del pulmón con alivio del broncoespasmo, más uniforme aereación alveolar y mejoría del tono muscular.

7.—Los efectos benéficos de la presión positiva intermitente, son más pronunciados en el bronchoespasmo, en la pérdida de la elasticidad-pulmonar y cuando la retención de secreciones constituyen factores enla producción de la incapacidad.

8.—Se discuten los detalles y las contraindicaciones del método.

RESUME

1.—Les troubles de la fonction dans les affections pulmonaires chroniques sont essentiellement liés à l'étendue de la sclérose, au degré de l'emphysème et à l'importance du bronchuospasme et de la rétention. Certains de ces troubles fonctionnels sont réversibles.

2.—La respiration en pression positive intermittente, associée aux aérosols bronchodilatateurs ou d'autre nature, est une méthode efficace de traitement des affections pulmonaires chroniques ayant déterminé des insuffisances ou des difficultés respiratoires.

3.—Les auteurs rapportent les résultats du traitement de 750 cas d'affections pulmonaires chroniques. Dans 5,1% des cas, il n'y eut pas d'amélioration, dans 13.8% il y eut une légère amélioration, dans 47,5% une amélioration moyenne, dans 33.6% une amélioration marquée.

4.—Les progrès cliniques se manifestèrent par une diminution de la dyspneé, une diminution de la toux et de l'expectoration, et l'augmentation des forces.

5.—On peut déterminer objectivement l'importance de l'amélioration en mesurant la capacité vitale et la capacité respiratoire maximum avant et après traitement. La capacité vitale se montre augmentée en moyenne de 7% après une série de traitement, de 14.9% après pulsieurs séries. Dans ces conditions respectives, on constata pour la capacité respiratoire maximum une augmentation de 15,8 et 28,5%.

6.—La respiration en pression positive intermittente provoque un soulagement et la disparition des symptômes grâce à une meilleure ventilation pulmonaire, un meilleur drainage bronchique, une meilleure distribution des aérosols dans l'ensemble du poumon dont il soulage le bronchospasme, une meilleure aération alvéolaire et une amélioration du tonus musculaire.

7.—L'effet heureux de la respiration en pression positive intermittente apparait plus nettement lorsque le bronchospasme la perte de l'élasticité et al retention restent réversibles.

8.—Les auteurs exposent les détails du traitement et ses contre-indications.

# Present Status of Aerosol Therapy with Proteolytic Enzymes: Studies on the Cytology of Bronchial Secretions

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Since the initial report[1] on the enzymatic lysis of respiratory secretions by the use of aerosol trypsin by two of the authors one year ago, continuing use of and investigation of this type of therapy has been carried out. It was necessary to determine whether the initially promising results could be confirmed when applied to a far larger number of clinical cases as well as to determine whether the therapy was applicable to other respiratory diseases than those first reported. Furthermore, it was felt equally important to determine whether any deleterious effects would result from prolonged administration. The material in this report in large part answers all three of these questions.

A brief review of the experimental background and the biochemical basis for enzymatic lysis of respiratory secretion is indicated. In vitro,

**TABLE 1.—*Viscosity-Lowering Effect of Trypsin * on Sputum as Measured by "Pipette Method"***

| Sputum Sample | Minutes of Digestion: 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|
| | Volume Flow, Cc. | | | | | | | | | |
| 1..... | 1.5 | 2.25 | 2.6 | 3.55 | 4.5 | 5.5 | 7.0 | 8.5 | 9.25 | 9.7 |
| 2..... | 1.8 | 2.6 | 3.3 | 4.0 | 5.3 | 6.6 | 7.8 | 9.1 | 9.8 | 9.9 |
| 3..... | 1.6 | 2.4 | 3.0 | 3.75 | 4.9 | 6.15 | 7.4 | 8.9 | 9.65 | 9.8 |
| 4..... | 1.7 | 2.5 | 2.9 | 3.7 | 4.8 | 6.0 | 7.4 | 8.85 | 9.5 | 9.8 |
| 5..... | 1.85 | 2.7 | 3.4 | 4.1 | 5.4 | 6.8 | 8.0 | 9.2 | 9.85 | 9.9 |
| 6..... | 1.75 | 2.5 | 3.1 | 3.85 | 5.0 | 6.25 | 7.5 | 9.0 | 9.75 | 9.9 |
| 7..... | 1.8 | 2.5 | 3.2 | 3.95 | 5.25 | 6.4 | 7.7 | 9.0 | 9.75 | 9.9 |
| 8..... | 1.65 | 2.35 | 2.8 | 3.6 | 4.70 | 5.6 | 7.1 | 8.6 | 9.45 | 9.75 |
| 9..... | 1.9 | 2.8 | 3.6 | 4.2 | 5.6 | 7.0 | 8.2 | 9.3 | 9.8 | 9.95 |
| 10..... | 1.7 | 2.4 | 3.0 | 3.8 | 4.95 | 6.25 | 7.5 | 8.9 | 9.7 | 9.85 |
| Average..... | 1.72 | 2.50 | 3.09 | 3.85 | 5.04 | 6.25 | 7.56 | 8.93 | 9.65 | 9.84 |

* Each sample of 25 cc. of sputum was subjected to 50,000 units of trypsin.

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FIGURE 1

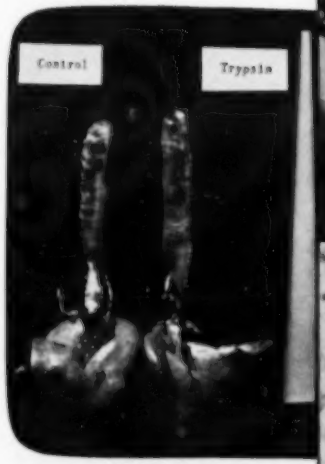


FIGURE 3

FIGURE 5

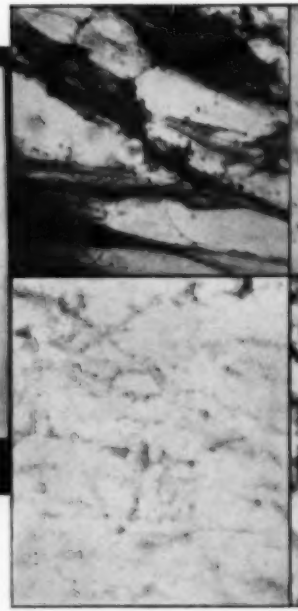

FIGURE 2

FIGURE 6

FIGURE 7

FIGURE 8

*Figure 1:* Sputum stained with mucicarmine, showing the lacy network of pink-staining mucous filaments.—*Figure 2:* Lysis of mucous filaments by tryptic action. This is the same sputum as shown in Figure 1 after being subjected to 15 minutes of digestion by 25 mg of trypsin at body temperature. Note that the strands of mucus have been completely disrupted leaving only pink-staining granular material.—*Figure 3:* A dog lung trachea preparation, showing transport of lamp blank by ciliary activity from the carina to thyroid cartilage in control animal and animal previously subjected to aerosol trypsin. Treated specimen shows lamp-black reached the thyroid cartilage more quickly than in the control animal.—*Figure 5:* Photomicrograph of cellular material in sputum of a patient subjected to 30 days of aerosol trypsin therapy, showing so-called "deep" cells, which may be mistaken for neoplastic, but are not.—*Figure 6:* Photomicrograph showing an area of squamous metaplasia in the wall of the casseous tuberculous cavity in a patient in the control group who had received no aerosol trypsin therapy.—*Figure 7:* Sputum from a tuberculous patient prior to aerosol trypsin therapy. Typical of the type and amount of cellular material including metaplastic cells noted in any tuberculous sputum.—*Figure 8:* Sputum from the same patient as shown in Figure 7. This specimen was taken after 30 consecutive days of aerosol trypsin therapy. No cellular material interpreted as neoplastic can be seen. Typical of all the patients in the test group.

50,000 units of crystalline trypsin produces a dramatic liquefaction of 25 cc. of thick sputum obtained from human patients. This lysis is reflected by the rapid decline in the sputum viscosity as measured by the method devised by Harris, Abrams, and Harris.[2] This effect is shown in table I.

The actual physical change in mucous can be best demonstrated by the microscopic comparison of sputum stained with mucicarmine, with the appearance of sputum which has been digested with trypsin before staining. The untreated slide, as shown in fig. 1, presents a lacy network of pink-staining mucous filaments. In fig. 2 it can be seen that tryptic lysis of the sputum has produced a complete disruption of the mucous strands which now appear as small, round globules of pink-staining material. Lytic action on the mucous fibril is brought about by the tryptic digestion of the protein portion of the mucin molecule.

Since any therapeutic agent, designed to treat diseases of the tracheobronchial tree must not in any way impair bronchial physiology, it was necessary to be absolutely certain that the application of crystalline trypsin did not impair ciliary activity, since the authors recognize the fact that adequate ciliary action is the most important normal mechanism for clearing the tracheobronchial tree of debris.

As previously reported, microscopic examination following the use of aerosol trypsin in the tracheobronchial tree as well as the lung parenchyma, revealed no deviation from the normal appearance. Ciliated epithelium was in no way changed morphologically. Based on the speed of transport of lamp black from the carina to the thyroid cartilage, no alteration in ciliary activity can be detected following the use of aerosol trypsin (fig. 3).

The method of administration remains essentially unchanged. The alternate method described in our initial report is now used exclusively. This consists of placing an "S" shaped baffle one-half inch in diameter between the glass oral tip and a standard vaponephrin-type nebulizer. A "Y" tube is inserted in the rubber tubing between the nebulizer and the oxygen tank. The baffle removes the large droplets which produce irritation of the vocal cords and soreness of the oral mucous membranes. During administration the patient regulates the oxygen flow to the nebulizer by placing the finger over the open end of the "Y" tube, during inhalation and removing it during exhalation.

It has been found that the best results are obtained by using 125,000 units dissolved in 2 cc. of Sorensen's phosphate buffer twice a day. The oxygen flow valve should be set for six liters per minute. It is still recommended that the patient be put on 50 mg. of diphenhydramine (benadryl) hydrochloride.

The clinical material on which the findings of this report are based is comprised of 152 patients who were treated with aerosol trypsin (table 2). These patients received a total of 1,856 individual aerosol treatments. The group included 45 with pulmonary tuberculosis; 23 with bronchiecta-

## RESULTS OF AEROSOL TRYPSIN THERAPY IN CERTAIN PULMONARY DESEASES

| Desease | No. of Cases | Average Dose daily in units | Average and maximum days | Criteria for good result | No. of good results | Percent |
|---|---|---|---|---|---|---|
| Tuberculosis | 45 | 250,000 | 14<br>30 | Reduced sputum volume and viscosity.<br>Reduced cough and bacterial count.<br>Increased vital capacity. Better sleep. | 42 | 93% |
| Bronchectasis | 23 | 250,000 | 4<br>10 | Reduced sputum volume and viscosity.<br>Conversion from purulent to mucoid.<br>Increased vital capacity. | 23 | 100% |
| Atelectasis<br>Post-operative | 9 | 250,000 | 1<br>3 | Re-aeration of involved lung. | 9 | 100% |
| Unresolved<br>Pneumonitis | 6 | 250,000 | 5<br>9 | Clearing of involved lung.<br>Increased sputum production.<br>Decreased viscosity.<br>Normal temperature. | 6 | 100% |
| Lung abscess | 3 | 375,000 | 12<br>21 | Closure of cavity. | 3 | 100% |
| Pulmonary<br>Emphysema c<br>Bronchitis | 29 | 250,000 | 5<br>14 | Decreased cough and sputum viscosity.<br>Increased tidal volume.<br>Normal temperature.<br>Increased exercise tolerance. | 24 | 82% |
| Bronchial<br>Asthma | 31 | 125,000 | 4<br>7 | Increased vital capacity.<br>Decreased cough and sputum viscosity.<br>Better sleep. | 27 | 87% |
| Fibro-cystic<br>Desease of<br>Pancrease | 6 | 125,000<br>to<br>250,000 | 2<br>7 | Decreased cough and sputum viscosity and volume.<br>Conversion of sputum from purulent to mucoid.<br>Increased vital capacity. | 6 | 100% |

TABLE II

sis; nine with post-operative atelectasis; six with unresolved pneumonia; three with chronic lung abscess; 31 with bronchial asthma; 29 with pulmonary emphysema and chronic bronchitis; and six with fibrocystic disease of the pancreas.

Before discussing the results in these 152 cases, it is best to restate the beneficial effects noted in aerosol enzymatic lysis. The immediate effects that have been routinely noted have been a tracheobronchial flushing, a thinning of sputum, an immediate increase in coughing followed by a marked decrease in coughing, which lasts from several hours to several days or longer, depending upon the completeness of the evacuation of the tracheobronchial tree. The gradual beneficial effects are, a conversion of purulent sputum to a clearer, thinner, less copious sputum, an increase in the vital capacity which has ranged from minimal to marked.

On the basis of these criteria, the present material confirms satisfactorily the good results obtained in our initial series of cases. To briefly summarize the results obtained in the diseases presented in our first report, based on this second group, we found that of the 45 cases of tuberculosis, 42 (93 per cent) manifested an excellent result, based on reduction of sputum volume, reduced bacterial count and reduction of cough, and decrease in toxicity. Of this group eight showed conversion of their sputum during the course of aerosol trypsin therapy.

### *Bronchiectasis*

Of the 23 with bronchiectasis, all manifested an excellent result based upon the conversion of sputum from purulent to mucoid, and on the decrease in the amount of sputum produced. Of this group three are inoperable, far-advanced bilateral cases of bronchiectasis, who have now been carried for approximately a year on intermittent aerosol trypsin therapy. This has reduced their sputum volume to almost normal amounts and has kept them practically symptom-free. The dosage has varied, depending upon the individual, from two days every week to two days every three weeks. One of these cases will be discussed in detail later in the paper.

It is our opinion that no other type of patient is as greatly benefited by aerosol trypsin therapy as the ones with chronic bronchiectasis which is too extensive for surgical cure. In these patients intermittent treatment with aerosol trypsin is superior to either aerosol or parenteral antibiotics, expectorants, or any combination thereof. In those whose bronchial tract is literally clogged with pus, the true physiologic debridement with trypsin is the treatment of choice.

### *Atelectasis*

Of the nine cases of post-operative atelectasis, all have shown excellent results, as manifested by clearing of the bronchial obstruction and reaeration of the atelectatic portion of the lung.

The effect of the treatment in this condition is rapidly achieved, often with one nebulization. An initial dose of 250,000 units may be used at

first. No more may be needed. The patient should be placed on intravenous sodium iodide after the obstruction has been digested.

### *Unresolved Pneumonitis*

Of the six patients with unresolved pneumonia, all have shown excellent results, based upon the resolution and clearing of the involved lung.

These cases represent a small but increasingly important group who fail to respond to antibiotics by resolution. Of the six treated, three were found to have pneumococci, one had Friedlander bacilli and two were nonspecific. These, together with those suffering from chronic inoperable bronchiectasis, represent the most important use of the therapy. Here too, an enzymatic debridement is achieved (fig. 4).

The second question which we hoped to answer by this present group of cases was that of further extension in the usefulness of the therapy. Based upon our initial results, it was felt that all cases of bronchopulmonary disease, manifested by chronic cough with marked sputum production, could possibly be benefited by enzymatic lysis of their respiratory secretions.

### *Lung Abscess*

Thus far, three cases of chronic lung abscess have been seen and treated by this method. They had had the disease for six, nine and 11 weeks respectively. All had been vigorously treated by at least two or more antibiotics, plus postural drainage or bronchoscopic aspiration. All three had continued to show marked sputum production and a febrile temperature curve despite this therapy. All three showed closure of the abscess cavity, normal temperature and cessation of sputum production after 12, 19 and 20 days of aerosol therapy respectively. This, we feel, represents a definite addition to the available methods of treating lung abscess.

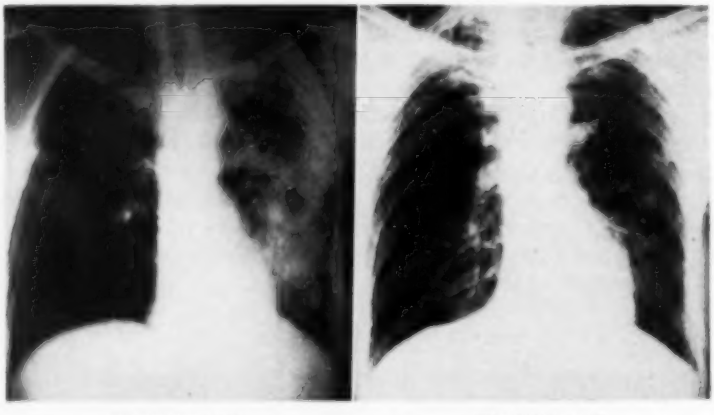

FIGURE 4 A FIGURE 4 B

*Figure 4A:* Roentgenogram of chest of case of unresolved Friedlander pneumonitis prior to aerosol trypsin therapy.—*Figure 4B:* Roentgenogram of chest of same patient following 10 days of aerosol trypsin therapy.

### *Bronchial Asthma*

There were 31 who had bronchial asthma in whom a significant amount of thick, tenacious sputum was a predominant factor. They were uniformly improved and given symptomatic relief by the administration of 125,000 units of trypsin, as an aerosol once a day. The duration of benefit varied widely. Some experienced decreased difficulty in respiration, lasting only two or three hours after treatment. In others the improvement was more striking. Bronchospasm was broken. They remained symptom-free until another attack occurred.

Twenty-seven of them showed enough improvement that we felt justified in classing them as good results. However, since asthma is primarily a bronchospastic disease and neither infectious nor primarily a derangement of bronchial secretory physiology, aerosol trypsin will never be a preferred method of treatment. It is, nevertheless, an addition to the treatment of asthma and, at such times as acute infection is superimposed, will be of great benefit. Periodic flushing of the bronchial tract by enzymatic lysis will be found to help in many cases.

### *Pulmonary Emphysema and Fibrosis with Chronic Bronchitis*

There were 29 in this group, which included some of the most gratifying results obtained in our present series of cases. In such patients with borderline pulmonary function, any method of clearing the tracheobronchial tree of debris and restoring a normal bronchial physiology is of benefit. Twenty-four of these patients showed a definite increase in tidal air and were able to increase their activity and return to more normal existence following four to seven days of aerosol trypsin therapy. This is well illustrated by the following:

*Case 62 (H. A.):* A 67 year old, white civil engineer had been suffering from pulmonary emphysema for the past seven years. Just prior to treatment he was almost completely confined to his home. He was only able to walk with assistance from his living room, where he had a temporary cot, to the door, where a car picked him up and drove him to his office. With assistance he was able to walk to the elevator and again, with assistance, walk from the elevator to his office. He had at one or another time received almost every conceivable form of treatment. When admitted to the hospital he showed a moderate temperature elevation to 99.8° F., had an almost incessant cough productive of fairly large amounts of rather gray, frothy, mucoid exudate. An x-ray film of the chest, in addition to far advanced pulmonary emphysema and fibrosis, showed an area of pneumonitis in the left lower lobe. He was placed on aerosol trypsin therapy, receiving 125,000 units twice a day for seven days. At the end of this time his cough had almost completely disappeared. The sputum production was minimal. He was discharged to his home when he was able to climb the stairs to the second floor for the first time in nine months. He maintained this improvement for six months. At the end of this time he again became short of breath and noticed a marked increase in sputum production and cough. He was readmitted to the hospital and was given five days of aerosol trypsin, taking 150,000 units twice a day. He again showed marked improvement in tidal air and was again able to resume a more normal activity. His last admission was seven months ago and he has not yet felt incapacitated enough to return for further treatment.

### *Fibrocystic Disease of the Pancreas*

There were six with fibrocystic disease of the pancreas included in this series of cases. The youngest was five and the oldest was 20 years of age. In all six, gratifying results were obtained by the use of aerosol trypsin.

In every case the vital capacity was increased, cyanosis was decreased, and the amount of sputum was markedly decreased. These patients were admitted with copious amounts of thick, ropey, tenacious bronchial secretion, which rapidly responded to enzymatic lysis.

*Preoperative Preparation for Chest Surgery*

Finally, one excellent use of enzymatic lysis of respiratory secretions was found during the course of this investigation. In preparing several of our bronchiectatic patients for operation, we found that the use of aerosol trypsin markedly cleansed the tracheobronchial tree preoperatively, reduced the amount of sputum and completely obviated the occurrence of spill-over to the contralateral lung. We have used this so successfully that we now feel, particularly in resectional surgery in tuberculosis, that a three day period of aerosol trypsin is an indicated part of the preoperative preparation. Each patient is given 125,000 units twice a day. The lobes removed at surgery following aerosol trypsin preparation show excellent cleansing of the entire bronchial tree in the removed segment.

The third and last phase of this investigation was to determine whether there were any further undesirable side-effects or any adverse reactions to the use of this form of therapy.

In the initial report, certain side reactions attendant upon aerosol trypsin administration were noted. In our subsequent work, no new side reactions other than those already described, have been noted. Those which were first reported were dyspnea and chills and fever. These two reactions were seen in approximately 5 per cent of the first series and approximately 7 per cent of the subsequent series. These tend to decrease and disappear as the therapy is continued. Thermal reactions are usually mild. They may be initiated with a chill, followed by a temperature elevation as high as 101° F. The chill may not be noticed initially and a gradual rise in temperature may occur six to 12 hours after the treatment is administered.

If the patients are routinely placed on one of the antihistaminics mentioned earlier in the paper, these thermal reactions seldom occur. At no time was the febrile reaction severe enough to interfere or necessitate cessation of the treatment.

Dyspnea was most frequently noted in those with low vital capacity and usually occurred at the end of, or shortly after the completion of treatment. It can be routinely and promptly relieved by the intravenous administration of 25 mg. of diphenhydramine hydrochloride. Those who manifest dyspnea to the initial treatment also rapidly develop a tolerance to the administration of trypsin.

The other side-effects must be mentioned, but the occurrence of these is only an indication of poor technique of administration. These are hoarseness and irritation of the mouth or nose. They indicate failure to rinse out the mouth and nasal passages after treatment has been administered. The occurrence of laryngeal irritation is present only when improper aerosolization has been used; that is, either too rapid admin-

istration or failure to use an "S" baffle tube between the nebulizer and the mouth.

During the past year the incidence of the above mentioned side-effects has been so small as to further convince us that they represent no real drawback to the enzymatic lysis of respiratory secretions.

*Cytologic Studies Following the Administration of Aerosol Trypsin*

During the past year a group of investigators, in a preliminary report not as yet published at this writing,[2] has reported the finding of certain unusual metaplastic cellular changes in the sputum of a small series of patients who had received aerosol trypsin. This has broached the serious question as to whether or not the administration of trypsin to the surface of the tracheobronchial tree is irritating enough to produce permanent cytologic changes of a neoplastic nature. This, of course, represents a real challenge to this form of therapy. It was therefore decided that a careful and painstaking investigation of this aspect of the problem would have to be undertaken.

The material to follow is a preliminary report of our investigation of this phase of trypsin therapy. This study is being continued and a separate report will be subsequently submitted for publication. In considering this problem it must at first be recognized that in most of the chronic lung disorders which have thus far been considered indications for aerosol trypsin therapy, metaplasia of the bronchial mucosa is one of the outstanding features of the pathologic picture of the disease. This is particularly true in bronchiectasis and tuberculosis. Therefore, any examination of the desquamated cellular material from these patients must demonstrate not merely the ordinary metaplasia observed, but a peculiar cellular change, which can be recognized as characteristic of patients treated by this material, or as frank neoplasia. It would also appear highly desirable that such a study be carried out on specimens of respiratory tract fluid aspirated by bronchoscopy, rather than on sputum. The cellular elements of sputum will include the cellular debris from the oro-pharynx as well as from the tracheobronchial tree and will therefore be misleading.

In our final report on this phase of the investigation, only bronchial aspirations will be included. However, the preliminary study to be presented hereafter was carried out, using cough specimens, since it was possible to obtain this material more quickly. This is also the type of material which was used in the report by the above mentioned investigators.

For our initial study two groups of patients with tuberculosis were selected in two different sanatoria. Both groups contained 30 patients. The first consisted of patients who were on all types of parenteral and oral therapy for tuberculosis, but who received no aerosol trypsin. The second consisted of patients who were given daily administration of 125,000 units of aerosol trypsin for a period of 30 days. A careful cytologic examination was made of the sputum from both groups at the beginning of the test period. The test group was then placed on aerosol

trypsin. At the end of 15 days a second cytologic study was made of the two groups and a comparison was made at this time. Again, at the end of 30 days, slides of the sputum were prepared, using the Papanicolaou technique and a second comparison carried out. Finally, two weeks after the cessation of trypsin, a third series of slides was made on the two groups and comparative studies again made. The cytologic comparison of the two groups prior to medication was essentially the same. The usual type and number of metaplastic cells noted in any tuberculous sputum were found (fig. 7).

At the end of the two week interval the comparison showed that the slides of the control group were essentially the same as those of the first examination. The slides from the test group were in comparison, approximately the same as those of the control group with the exception that there was less cellular debris of all types. There was no evidence, however, of any unusual cell morphology which could not be seen in the control group. This same comparison was found to hold true at the end of the 30 (fig. 8), and at the end of the 45 day period.

At the completion of this initial phase of the investigation it is our opinion that the administration of aerosol trypsin endobronchially, produces no unusual change in the cytology of the oropharynx and tracheobronchial tree.

One in the test group at the 30 day examination showed some so-called "deep cells" in his sputum (fig. 5). These might be mistaken for neoplastic cells, but are considered to be evidence of desquamation of cells of the deeper layer of an area of squamous metaplasia. They are not neoplastic and were not found at the 45 day examination.

At the end of the test period, several patients in both groups underwent resectional surgery. The specimens removed were carefully studied and microscopic sections of the bronchial tree obtained from members of both groups. A careful study of these specimens also gives no evidence whatsoever of any unusual metaplasia in the test group, not within the limits of expectation of the control group (fig. 6). In addition to the test group described above, cytologic studies were made on the sputum of several of the group of bronchiectatic patients, who have been carried on intermittent aerosol trypsin over the period of the last year. All of these patients had been receiving aerosol trypsin for at least six months, no less frequently than two days out of every three weeks. The cytologic examination of their sputum failed to reveal any unusual metaplasia of the cellular elements, pointing toward any type of neoplastic change.

We feel that this last mentioned examination is such as to rather conclusively prove the safety of this type of treatment. The history of one of these cases is sufficiently interesting, both from the standpoint of treatment of one of the diseases amenable to aerosol trypsin therapy, and to the question of metaplastic change to be given herewith.

*Case 76 (T. P.):* A white female, aged 27, was first admitted to the hospital on November 30, 1951, when a diagnosis of bilateral chronic saccular bronchiectasis was made. Bilateral lobectomy was advised and on December 4, 1951 left thoracotomy was performed and left lower lobectomy accomplished. Post-operatively she made a satis-

factory immediate convalescence, with re-expansion of the upper lobe. At the time of discharge, the upper lobe was fully expanded and only a small fluid level was present above the diaphragm. However, two weeks later she was seen to have complete spontaneous collapse of the left upper lobe, and a considerable early fibrothorax. She was readmitted to the hospital on January 28, 1952 and an attempt was made at decortication and re-expansion of the left upper lobe. She had such severe and uncontrollable bleeding that this operative procedure had to be stopped before completion and the chest wall closed. Subsequent to this she developed a large bronchopleural fistula and empyema. This was treated with intrapleural instillation and irrigation of solution of crystalline trypsin and Sorensen's phosphate buffer. The bronchopleural fistula rapidly closed, the lung re-expanded fairly satisfactorily, but at the completion of treatment, a fixed left upper lobe with a small fibrothorax was found to be the end result. Because of this it was felt that any attempt at lobectomy on the right side would be hazardous. Although her sputum production was approximately halved by the left lower lobectomy, she still had a copious production of a foul, yellow, purulent sputum from the bronchiectasis on the right side. This could be decreased slightly in amount and made less offensive in odor by the intermittent use of aerosol penicillin and streptomycin. However, a chronic, productive cough remained.

On June 24, 1952 she was placed on aerosol trypsin 150,000 units twice a day for two days. At the end of this time her sputum production had almost stopped and what sputum was raised, was clear white. Since that time she has been carried on aerosol trypsin therapy, giving her intermittent courses of the medication whenever the amount of sputum production increases and changes to a purulent character. During the past year she has been able to keep her sputum production at a minimum and free of pus by taking 125,000 units twice a day for two or three days at intervals of about three weeks.

### *Evaluation*

After one year of using this form of therapy, we feel that our initial satisfactory results have been substantiated. Aerosol trypsin represents a worthwhile addition to the armamentarium of the chest internist and surgeon alike, in the treatment of those acute and chronic disorders of the lung associated with increased amounts of tenacious respiratory tract secretion and debris. Its mucolytic action has been amply demonstrated both in vitro and in vivo. However, we feel that the beneficial results to be obtained from the use of aerosol trypsin are greater than the mere lysis of tenacious mucoid bronchial secretion, which can be obtained by several other methods, including aerosolized detergents. This added advantage of aerosol trypsin lies in the fact that it is in the true sense an enzymatic debridement, which can be applied to the entire respiratory system. Its action in the pulmonary system is therefore in every way similar to its action on the body surface and in body cavities in that it actually digests all protein debris, not only liquefying mucous, but also digesting purulent exudates, promoting a serous out-pouring from granulating surfaces, cleaning up granulating areas, and promoting the regeneration of surface or pavement epithelium.

This debriding action can be most clearly demonstrated in those cases of unresolved pneumonitis which have shown remarkably satisfactory clearing under aerosol trypsin management. It is also evidenced by the manner in which inoperable cases of bronchiectasis can be maintained in a state of freedom from sputum and freedom from purulent secretion over prolonged periods of time by a short treatment of aerosol trypsin. Thus, the most prolonged benefits of treatment of this type have been obtained in bronchiectasis, unresolved pneumonia, pulmonary emphysema with chronic bronchitis, fibrocystic disease of the pancreas, and lung

abscess. The benefits in bronchial asthma, while partially satisfactory in the majority of cases, have, been only temporary. The use of aerosol trypsin as a method of cleansing and preparing the tracheobronchial tree for resectional surgery, has been one of the greatest improvements resulting from our investigation. Its use is to be unqualifiedly recommended in the preoperative preparation of all patients in whom pulmonary surgery is contemplated. The untoward side-effects are minimal and, in nearly 2,000 individual administrations of the material by the aerosol method, we have had no serious reaction or complication. It is therefore to be considered an eminently safe form of therapy.

An evaluation of any unusual metaplastic tendency from this treatment is as yet incomplete, but thus far we do not feel that any evidence points to the fact that its use is dangerous in this respect.

## SUMMARY

An evaluation of aerosol trypsin therapy based on one year's use in 152 cases and 1,856 individual administrations has been completed. It was found that aerosol trypsin is an eminently satisfactory agent to lyse mucous. It has been used with benefit in pulmonary tuberculosis, bronchiectasis, post-operative atelectasis, unresolved pneumonia, lung abscess, bronchial asthma, pulmonary emphysema, chronic bronchitis and fibrocystic disease of the pancreas. It has been found a valuable adjunct in the preparation of patients for pulmonary surgery. Its side-effects are minor and of insignificant occurrence. On the basis of preliminary studies, it does not produce metaplasia, which is in any way characteristic or suggestive of neoplasia.

## RESUMEN

Se ha llevado a cabo una estimación del valor del aerosol detripsina que se administró a 152 personas durante un año, con 1.856 aplicaciones durante ese tiempo. Se encontró que al aerosol de tripsina es un agente eminentement satisfactorio para lisar la mucosidad.

Se ha visto que es benéfico en tuberculosis pulmonar, bronquiectasia, atelectasia postoperatoria, neumonía no resuelta, absceso pulmonar, asma bronquial, enfisema pulmonar, bronquitis crónica yenfermedad fibroquística del páncreas. Se ha encontrado también que es un valioso adyuvante en la preparación de los enfermos para cirugía pulmonar.

Sus efectos colaterales son menores y de frecuencia insignificante.

Basándose en los estudios preliminares no produce metaplasiaque sea de cualquier manera característica o sugestiva de neoplasia.

## RESUME

Les auteurs ont établi le bilan complet du traitement par les aérosols de trypsine en se basant sur leur utilisation pendant un an pour 152 cas et un total de 1856 administrations individuelles. Ils ont constaté que les aérosols de trypsine sont un agent extrêmement satisfaisant quand il s'agit de provoquer la destruction d'une atteinte de la muqueuse.

Ils ont été employés avec profit dans la tuberculose pulmonaire, les

bronchiectasies, l'atélectasie post-opératoire, la pneumonie non résorbée, l'abcès du poumon, l'asthme bronchique, l'emphysème pulmonaire, la bronchite chronique et la maladie kystique du pancréas. Ils se sont trouvés être un adjuvant précieux dans la prèparation des malades à la chirurgie pulmonaire. Leurs inconvénients sont faibles, et sont rarement notés. En se basant sur des études préliminaires, les auteurs pensent qu'ils ne provoquent pas de métaplasie qui puisse être caractéristique ou évocatrice de néoplasie.

## REFERENCES

1 C. R. Limber; H. J. Reiser; L. C. Roettig; G. M. Curtis, "The Enzymatic Lysis of Respiratory Secretions by Aerosol Trypsin," J.A.M.A., 149:816, 1952.

2 Farber, Seymour. Paper presented before the Interim Session, American College of Chest Physicians, December, 1952. (Not yet published.)

# Simple Spontaneous Pneumothorax*

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Riolan[1] (1648), Littre[2] (1713), Meckel[3] (1759) and others in the 18th and 19th centuries reported air in the pleural cavity following trauma. In 1803 Itard[4] called attention to five cases found at necropsy. He coined the term pneumothorax. Laennec[5] (1819) discussed the clinical aspects of this condition and its recognition by physical examination. The writings of these authors alerted physicians and many reported cases. In fact, just a century after Itard's thesis was published Emerson[6] listed 358 literature references to this condition. During the past 50 years a vast bibliography has accrued with ever increasing knowledge of frequency, etiology, diagnosis and treatment.

Air may reach a plueral space through the parietal pleura as in stab or bullet wounds or disease which penetrates the chest wall. Perforation of esophageal or gastric ulcers and subphrenic abscess may be responsible. Most frequently air is found in the pleural cavity as a result of willful induction in the treatment and diagnosis of disease.

Air may also enter a pleural cavity through the visceral pleura. Anything that establishes a communication between bronchial ramifications or air cells and the pleural space permits this endogenous origin of air in the cavity. Injuries to the chest wall sometimes result in rib fragments penetrating the visceral pleura. Needling the chest for any purpose such as aspiration of fluid may puncture the visceral pleura. Resuscitation of newborn infants, passing a bronchoscope, administering intratracheal anesthesia, etc., are sometimes responsible.

Hewson[7] (1767) apparently was first to mention the possibility of entry of air into a pleural space through perforation of pulmonary diseases. It is now known that both acute and chronic disease may so damage the visceral pleura as to permit the escape of air into the pleural space.

The term *spontaneous pneumothorax* has been reserved for those cases in which disease or defect of the pleura permits air from the lung to enter the pleural space. Earlier in the evolution of our knowledge of spontaneous pneumothorax this condition was usually recognized in persons who had pulmonary disease demonstrable during life or at necropsy. More cases were reported due to pulmonary tuberculosis than to any other disease, probably because of its prevalence and inadequacy of differential diagnostic procedures so that many nontuberculous pulmonary

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conditions were classified as tuberculous. Biach[8] (1880) collected 986 cases of spontaneous pneumothorax from the literature and from the records of three Vienna hospitals and found tuberculosis reported as responsible in 77.8 per cent. As late as 1931, Palmer and Taft[9] stated that among adults from 80 to 90 per cent of the cases of spontaneous pneumothorax were due to tuberculosis.

Observations were made to determine frequency of spontaneous pneumothorax among persons with pulmonary tuberculosis. Biach[8] reported that it had been recognized in 1 per cent of 58,731 cases. Weber[10] stated that at necropsy spontaneous pneumothorax was found in 10 per cent of tuberculous persons. With more extensive use of x-ray inspection Barlow and Thompson[11] called attention to the frequency of small pneumothoraces which without this diagnostic advantage were usually not detected during life.

For the first two or three decades of this century it was still generally believed that spontaneous pneumothorax nearly always indicated the presence of pulmonary tuberculosis. Even if this disease could not be located after expansion of the lung the individual was strongly advised to have at least one year of bed rest. So certain were physicians that pulmonary tuberculosis must be present that in many instances spontaneously collapsed lungs were kept collapsed artificially for a year or more.

As time passed there was an increasing number of persons reported with spontaneous pneumothorax who did not react to tuberculin, tubercle bacilli were not recovered and no evidence of tuberculosis was then or later obtainable. Since the cause was not determined this condition was referred to as *idiopathic spontaneous pneumothorax.*

This was frequently seen in young adult males who remained in good health so there were few opportunities to make postmortem examinations. However, in 1932 and 1933 Kjaergaard[12, 12a] reported five of his own cases and six others from recent literature in which he described the etiology. In one type a valve is formed by emphysematous tissue, in another by congenital valve vesicle and in the other by scar tissue. He designated the condition spontaneous pneumothorax simplex. Kjaergaard pointed out that frequently spontaneous pneumothorax in an apparently healthy person has no relationship to tuberculosis. He expressed the opinion that individuals with this condition should be spared loss of time and expense of sanatorium treatment as well as fear of tuberculosis.

Kjaergaard's observations have been adequately confirmed and it is now recognized that simple spontaneous pneumothorax is usually due to congenital or acquired defects in the lung or pleura resulting in emphysematous blebs (bullae, air vescicles, etc.) which rupture in one or more places so that air gains admission to the pleural space. Adhesions between the parietal ad visceral pleurae may also result in rents in the latter.

In 1934 Hamman[13] described spontaneous interstitial emphysema of the lungs. He believed it was due to rupture of pulmonary alveoli with the escape of air into interstitial tissues. The cause of this condition was

not known, but he suggested that an alveolar wall here and there may become attenuated and weakened without known reason. This could be due to developmental defects, previous disease or present disease too slight to be detected. In any event, when a large amount of air escapes in this manner it may dissect along the connective tissue bands surrounding blood vessels and form blebs on the pleura, which in turn may rupture and cause spontaneous pneumothorax.

In 1934 we[14] reported 31 cases of spontaneous pneumothorax, 10 of whom had apparently responsible pulmonary disease. Two had bronchial asthma and 19 were classified as the simplex type. We have since seen many persons with spontaneous pneumothorax presumably caused by various pulmonary diseases including malignancies, silicosis, tuberculosis, etc. In our group there have been those with traumatic pneumothorax produced by bullets, inadvertent opening of pleura during surgical operation, bronchoscopy, pitchfork tine, chest injury in autombile accidents, etc.

In this paper only cases of simple spontaneous pneumothorax are presented. This group includes 123 persons of whom 18 were preliminarily reported in 1934. Of the 123, eight were disqualified because of incomplete or lost records.

The ages of these 115 persons at the time of the first diagnosed attack are shown in *table 1*. Only one infant was seen (not included in table 1

TABLE 1
AGE AT TIME OF FIRST DIAGNOSED ATTACK

| | | | |
|---|---|---|---|
| 15-19 | 13 | 40-44 | 5 |
| 20-24 | 55 | 45-49 | 0 |
| 25-29 | 16 | 50-54 | 1 |
| 30-34 | 15 | 55-59 | 2 |
| 35-39 | 7 | 60-64 | 1 |

because of incomplete record) and the etiology of the pneumothorax was not determined. Pneumothorax has been reported in several infants, including new born babies. The first newborn case was described by Rugi[14a] in 1878. Factors interfering with normal respiration causing emphysema and too vigorous resuscitation appear to have been the chief causes.

The highest incidence in our group occurred between the ages of 20 to 24 years with 55 (47.8 per cent) cases. In fact, 73 per cent of our cases first occurred between the ages of 15 and 29 years. This age incidence has been a common observation of numerous authors but no entirely satisfactory explanation has been offered. Only 31 in our group occurred after the age of 29 years and only 16 in persons older than 34. The oldest was 64 years.

Numerous authors have observed much more frequent occurrence of simple spontaneous pneumothorax among males than among females. In this group 98 (85 per cent) are males and 17 are females. This sex difference has not been satisfactorily explained.

Among the 115 cases here reported spontaneous pneumothorax occurred on the left side in 64, the right side in 42 and bilaterally in nine.

### *Diagnosis*

*Symptoms* at onset vary from those unrecognized by the individual to those of extreme severity. In two of our cases pneumothorax was found while they were being examined for other reasons with no symptom having been experienced when the collapses occurred.

In 78 (67.8 per cent) individuals the first symptoms were severe enough to impress them with the exact time when the condition happened. Most frequently the initial symptom was sharp pain. This occurred over various parts of the involved side of the chest, including upper and lower axillae, precordium, shoulder and in some cases substernal regions. Not infrequently the pain radiated down the arm and in a few the arm felt numb. In some cases the initial pain was excrutiating and in one it was localized over the epigastrium.

Usually pain preceded dyspnea. In some cases severe dyspnea did not occur. In other shortness of breath was the first symptom with or without subsequent pain. One stated that he felt his air was suddenly shut off —pain followed.

A man of 39 years was watching a parade. As he turned to leave sudden excruciating pain on the right side of his chest made him believe he had "been shot." Shortness of breath followed and by the time he reached his hotel one block away he was unable to speak to the clerk, who immediately placed an emergency call for a physician.

In one patient pain and dyspnea were so severe that he suddenly fell to the floor in shock. In another the pain in the right axilla extended down the right arm which became numb, he perspired profusely and became weak and shaky. A third also described symptoms of shock.

In only two cases were chills and fever present immediately preceding or following the attack. Although spontaneous pneumothorax has accompanied pneumonia, no evidence of this disease was found in these persons.

In two cases, positive intrapleural pressure developed so rapidly that the individuals were near death at the time they were first seen, with respiratory rates approximately 50 per minute, pulses practically imperceptible and marked cyanosis.

In most of our cases severe symptoms began to subside within a few hours and soon disappeared. However, occasional chest pains occurred for several weeks to a few months and in some for years following the initial attack.

In the remaining 35 the onset was gradual. The first symptoms experienced were mild such as slight aching in a shoulder, mild chest pain on changing posture or occasionally on respiration, a feeling of oppression or slight pressure on the involved side. One experienced only dizziness. Three described gurgling in their chests. A considerable number of these persons did not consult physicians for several days or more than a week after the first mild symptoms appeared.

No symptom is pathognomonic for simple spontaneous pneumothorax. However, in every person who presents the symptoms above enumerated whether with gradual or sudden onset, this condition should be considered.

Activity of the individual at the time of onset affords no help in diagnosis. *Table 2* reveals a large variety of activities at the time the first

TABLE 2
ACTIVITY AT TIME OF ATTACK

| | | | |
|---|---|---|---|
| No unusual activity | 26 | Washing hands | 1 |
| Sleeping | 10 | Working on scaffold | 1 |
| Time unknown | 2 | Hooking casting | 1 |
| Arising in morning | 4 | Running | 3 |
| Eating breakfast | 4 | Lifting | 7 |
| Sitting | 5 | Climbing hill, stairs, ladder | 4 |
| Standing quietly | 4 | | |
| Riding | 4 | Immediately after | |
| Doing laboratory experiment | 1 | bicycling | 1 |
| Painting stencil | 1 | physical ed. class | 1 |
| Developing photo print | 1 | wrestling | 1 |
| Studying in bed | 1 | playing trombone | 1 |
| Walking | 12 | | |
| Fixing furnace 2 AM | 1 | Coughing, laughing, sneezing, | |
| Shaving | 1 | asthmatic attack | 5 |
| Brushing teeth | 1 | Not recorded | 11 |

symptoms were noticed. In 26 the onset was so gradual it was not associated with any particular activity. Two did not know when the attack occurred. These individuals could think of nothing unusual they were doing at the time of the initial attack. Ten were awakened from sleep with pain in the chest. In fact, 31 were engaged in slight activity and only 25 were doing or immediately before were engaged in more strenuous work such as lifting, climbing and coughing. In 11 cases our records do not contain this information.

The findings on *conventional physical examination* depend upon such factors as degree of collapse and how soon the individual is seen. In severe cases examined within an hour or so after onset, inspection reveals evidence of cyanosis, anxious expression, and in some signs of shock. Respiratory rate is accelerated and the movements of the chest wall on the involved side are definitely limited. If intrapleural positive pressure is present, the intercostal spaces may bulge. At the opposite extreme when only a small amount of air has reached the pleural space the only finding on inspection may be slight limitation of movement of the chest wall.

Percussion of the chest with an underlying extensively collapsed lung usually reveals a resonant or even tympanitic note. When there is marked

tension the chest wall acts like an overstretched drum and cannot vibrate. Thus, the percussion note becomes muffled and at time approaches dullness. In small pneumothoraces there may not be enough air present in the pleural space to alter the percussion note.

When the lung has collapsed to 50 per cent or more of its volume breath and voice sounds are usually faint or entirely absent on auscultation. In small pneumothoraces all auscultatory findings may be normal.

The conventional physical examination is of almost no aid when small amounts of air such as 200 to 300 cc. are present in the pleural space.

*Fluoroscopic and x-ray film inspection* of the chest play an important role in detecting unsuspected and confirming questionable cases and determining the degree of collapse as well as any appreciable displacement of the mediastinum and diaphragm. X-ray inspection reveals a mantle of decreased density at the periphery of the lung with absence of lung markings and demarcated from the atelectatic lung margins. When only a small amount of air is in the pleural space it may be completely overlooked by x-ray inspection. Again air may be pocketed in front or back of the lung so it is not visualized on the usual posterio-anterior exposure. All of the cases here reported were plainly in evidence on x-ray films.

Among our 115 cases, in the initial attack the degree of collapse was less than 25 per cent in 15. *(Table 3)* In seven the collapse was approxi-

TABLE 3
DEGREE OF COLLAPSE

| Number | Per Cent |
|---|---|
| 15 | Less than 25 |
| 7 | 25 |
| 8 | 33 |
| 7 | 40 |
| 33 | 50 |
| 11 | 60-75 |
| 34 | 100 |

mately 25 per cent; in eight 33 per cent; in seven 40 per cent; in 33, 50 per cent, in 11 from 60 to 75 per cent; and in 34 the collapse was complete.

The diagnosis of simple spontaneous pneumothorax is made by correlation of history, conventional physical signs and x-ray shadows. In some cases one or more of these is misleading and therefore differential diagnosis may be difficult. From symptoms alone simple spontaneous pneumothorax has been diagnosed as pneumonia, intercostal neuralgia, pleurisy, coronary disease, acute heart failure, pericarditis and even perforated gastric lesions. All of these conditions were diagnosed or considered in some of the persons of this group before the final diagnoses were made.

The findings on conventional physical examination may be confused with those of large pulmonary cavities, marked upward displacement of

one side of the diaphragm, with large collections of gas in the digestive organs, diaphragmatic hernia, gaseous sub-diaphragmatic abscess, pulmonary aplasias and pulmonary cysts.

Various x-ray procedures aid in differentiating between some of these conditions. However, there are those, particularly lung cysts, that cannot be differentiated from simple spontaneous pneumothorax by this method. In such cases thoracotomy is necessary to determine the actual condition.

Prognosis in uncomplicated simple spontaneous pneumothorax is excellent from the initial attack since the lung usually reexpands from within a few days to a few weeks. Prognosis can become exceedingly grave when extensive and prolonged bleeding occurs within the pneumothorax cavity or when positive air pressure develops. Subsequent to simple spontaneous pneumothorax, five of our patients died from other causes; one, from cerebral hemmorrhage at the age of 22 years. One died in an accident at the age of 19 years, two from malignancy both at the age of 48 and, one, a United States marshall, was shot at the age of 47 by a prisoner (Reported by A. A. Wohlrabe, Minn. Med. 15:182, 1932). Of all of our patients traced to date, none has died from spontaneous pneumothorax or its complications.

### *Treatment*

In the earlier years of our work many physicians still entertained the belief that most persons with spontaneous pneumothorax were tuberculous even though pulmonary lesions could not be demonstrated; therefore bed rest for at least one year was recommended. This was employed for our first patient in 1923 *(Table 4)*.

TABLE 4

| TREATMENT | No. |
|---|---|
| No hospital or bed rest | 41 |
| Hospital or bed rest 1 week or less<br>Average 4.7 days | 26 |
| Hospital or bed rest more than 1 week<br>Average 19.9 days | 35 |
| Hemothorax<br>Average 26 days | 9 |
| Bed rest one year | 1 |
| Sanatorium and artificial pneumothorax | 1 |
| Artificial pneumothorax at home | 1 |
| Surgery | 1 |

Forty-one had no hospital or bed rest but were advised to reduce physical activity to a minimum until their lungs reexpanded. Twenty-six were in bed in hospitals or homes for one week or less. The average was 4.7

days. Thirty-six were on bed rest in hospitals or homes for more than one week. The time ranged from eight to 50 days with an average of 19.9 days. In nine with hemopneumothorax the period of confinement to bed ranged from four to 60 days with an average of 26 days. One of our early cases was on bed rest for a year (1928). Two had bed rest and artificial pneumothorax at home (1928 and 1930). One was sent to a sanatorium where the collapse was continued by artificial pneumothorax (1943) and one had surgery (1951).

Many cases of simple spontaneous pneumothorax require no treatment except sedation at the beginning and reduced physical activity. For others bed rest at home or in a hospital is advisable for a few days to a few weeks depending upon degree of collapse and rate of reexpansion. The pleural rent soon closes and the lung reexpands without incident in most cases. As the lung reexpands activity may be increased gradually and the majority of cases treated by bed rest are able to resume normal living in a few days to a few weeks. Throughout the reexpansion period the individual should be instructed to report promptly the appearance of any symptom such as pain, shortness of breath or pressure. Frequent fluoroscopic or x-ray film inspections should be made until the lung appears to be completely reexpanded.

In uncomplicated cases aspiration of air either by needle or catheter is neither indicated nor advisable. The creation of abnormal negative pressure in the pleural cavity may keep the pleural rent open.

*Table 5* shows the approximate time required for lungs to reexpand following first attack of simple spontaneous pneumothorax. The time was

TABLE 5

| TIME REQUIRED TO REEXPAND | No. |
|---|---|
| 10 days | 3 |
| 2 weeks | 14 |
| 3 | 34 |
| 4 | 29 |
| 6 | 15 |
| 7 | 3 |
| 2 months | 7 |
| 3 | 1 |
| Surgery | 1 |
| Cont'd. on pneumothorax | 3 |
| Unknown | 5 |

not determined in four because pneumothorax was continued artificially or surgery was performed. The time is not known in five because we were unable to trace them or x-ray films of the chest were not made at sufficiently short intervals. Of the remaining 106, 10 days was the shortest time and the longest was three months.

*Complications*

*Pleural Fluid.* In the 115 cases no pleural fluid was seen in 72. Enough accumulated to be detected by x-ray inspection in 43 of whom 39 had only a small amount. There were three with moderate accumulations which absorbed within a few days without removal. One had a large effusion. This man of 21 years developed simple spontaneous pneumothorax in January, 1951 which was soon followed by chills and fever. Eight days later 1500 cc. of cloudy yellow fluid was removed from the left pleural space (reported sterile). A catheter attached to a Stedman pump was introduced one week later and continued for approximately a month. During this interval streptokinase and streptodornase were introduced on three different occasions. He was hospitalized 51 days. The only residuals now in evidence are obliteration of the left costophrenic angle and thickened pleura over the apex of the left lung.

When fluid in small or larger amount does not absorb promptly it should be removed by needle or catheter as frequently as necessary to keep the pleural surfaces as dry as possible. Otherwise the lung will not reexpand promptly and fibrin is likely to deposit on the pleural surfaces, greatly delaying and even preventing reexpansion after which decortication may be necessary.

*Hemopneumothorax.* Occasionally when the visceral pleura ruptures blood vessels are torn with bleeding into the pleural cavity. This may be in small or large quantities. In all cases of *hemopneumothorax* blood should be aspirated. If the hemorrhage persists unduly long or a dangerous amount of blood is being lost, bleeding points should be closed surgically and at the same time the rent in the pleura repaired. In severe cases blood transfusions may be necessary.

Spontaneous hemopneumothorax occurred in nine of our cases as follows:

1. A man of 24 years had spontaneous hemopneumothorax discovered on January 2, 1930. Needle aspiration was performed on several occasions. He was hospitalized 50 days. The collapse was artificially maintained for several months. The only residual now in evidence is obliteration of the left costophrenic angle.

2. This man of 34 years was admitted to a hospital November 14, 1930 with tension hemopneumothorax. Large amounts of blood and air were aspirated. He was transferred to a veterans hospital but complete study revealed no evidence of tuberculosis. He had no further chest trouble, but died March 14, 1948 from carcinoma of the prostate with metastases.

3. A man of 23 years was found to have spontaneous hemopneumothorax on April 26, 1941. Blood was aspirated on three successive days —a total of 2500 cc. He was on bed rest at home for two weeks. His chest now appears normal.

4. A man of 39 years was admitted to a hospital on October 23, 1941 with spontaneous hemopneumothorax. Bloody fluid was aspirated 10 times. He was hospitalized 26 days. His chest now appears normal except evidence of slight thickening of the pleura over the entire left side.

5. A man of 31 years developed spontaneous hemopneumothorax September 12, 1944. Two days later 1100 cc. of bloody fluid was removed from the right pleural cavity. On September 27, 1600 cc. of dark brown thin fluid was aspirated. Oxygen was prescribed for dyspnea and one blood transfusion was given. He had a mild recurrence in 1946 and has since remained well.

6. A girl of 17 years developed spontaneous hemopneumothorax on January 22, 1948. Blood was aspirated on three occasions, a total of approximately 2000 cc. She was hospitalized 26 days and her lung was reexpanded in about three months. Her chest now appears entirely normal by all phases of the examination. (This case was reported by Dr. G. J. Kertesz, Journal-Lancet, 70:143, 1950.)

7. A man of 20 years was found to have spontaneous hemopneumothorax on March 31, 1948. Blood was aspirated from the left pleural cavity on two occasions, a total of 700 cc. He was hospitalized 12 days. His chest now has an entirely normal appearance.

8. This man of 34 years developed spontaneous hemopneumothorax on July 11, 1949 on the right side. One thousand cc. of sanguinous fluid was aspirated. He was hospitalized 18 days and the lung was expanded in three weeks. The only demonstrable residual is partial obliteration of the right costophrenic angle.

9. A man of 31 years developed right spontaneous hemopneumothorax on August 31, 1951. He was treated surgically September 14 and has remained well.

*Tension Pneumothorax.* Occasionally when pleural rupture occurs, a flap remains which acts as a one-way check valve. Thus air enters the pleural space on inspiration, but closure of the valve prevents its escape on expiration with the development of positive pressure. This situation immediately becomes an emergency as pressure may result in marked mediastinal displacement with severe embarrassment of respiratory and cardiac function. If the condition is not recognized death can occur in a short time.

If diagnosis is made in time, prompt relief is observed by thrusting an 18-gauge needle through the chest wall. Enough air escapes to reduce remarkably the pressure in a few seconds. It may then be necessary to pump air from the pleural cavity but high negative intrapleural pressure should be avoided. After the initial aspiration the patient must be kept under constant observation for pressure symptoms. If these occur other aspirations may be necessary. In some cases, after the needle is removed air accumulates so fast and aspirations are required so frequently that an indwelling needle or catheter and check valve are advantageous to provide continuous escape of air until it no longer accumulates sufficiently to cause pressure. At all times high negative intrapleural pressure should be avoided.

If the lung does not reexpand and positive pressure continues to develop after aspiration is discontinued it may be necessary to close the opening in the visceral pleura surgically. This also applies to lungs that

do not reexpand with reasonable promptness in the absence of positive intrapleural pressure. In such cases the pleural openings may be so large that they will not close spontaneously and chronic pneumothorax results.

Serious tension with the initial attack occurred in only two cases in our group. One had hemopneumothorax and the other simple spontaneous pneumothorax. The pressure symptoms were so extreme that passage of a needle into the pleural space apparently was life saving. In two other cases air was removed when mild pressure symptoms appeared. The degree of collapse is not an indication for removal of air. In our 34 cases of complete collapse of one lung air was aspirated in only four because of evidence of positive intrapleural pressure. The remaining 30 reexpanded satisfactorily. However, blood was aspirated in all who had spontaneous hemopneumothorax and fluid was removed from one with a large volume of nonsanguinous accumulation.

*Tuberculosis.* In our 115 cases, 41 had tuberculosis as manifested by the tuberculin reaction. However, in none of them was there evidence of clinical lesions at the time of or immediately after the lungs had reexpanded. There was no reaction to tuberculin in 71 indicating total freedom from tuberculosis. The result of the tuberculin test was not recorded in three.

Three of the group of 115 subsequently developed clinical tuberculosis. One at the age of 20 years in 1923 had spontaneous pneumothorax on the left side. There was a history of exposure to tuberculosis in the family and he was a reactor to tuberculin. When the lung reexpanded no evidence of clinical disease could be detected. Nevertheless he was placed on bed rest for one year after which he gradually resumed complete activity. Five years after pneumothorax had occurred, he was found to have moderately advanced disease in the upper lobe of the left lung with tubercle bacilli in his sputum. Apparently adhesions had not formed following the spontaneous pneumothorax and an excellent collapse of this lung was obtained artifically. He made an excellent recovery. Later a lesion appeared in the upper lobe of the right lung. This was treated successfully. He has remained well, worked regularly and in 1952 he was accepted for life insurance.

A man of 24 years who had spontaneous hemopneumothorax on the left side in 1930 and was treated successfully presented no evidence of clinical tuberculosis although he reacted to tuberculin. In 1935 he was found to have moderately advanced tuberculosis in the right lung which was promptly treated successfully.

A man of 19 years had spontaneous pneumothorax on the left side in February 1928. He did not react to tuberculin and no evidence was found of disease after his lung reexpanded. In the fall of 1942 he shared a hotel room for about three weeks with a man who was later found to have active tuberculosis. X-ray film inspection in 1945 revealed no evidence of disease. The tuberculin test was not administered until 1946 when he was found to be a reactor at the age of 37 years. He then had active tuberculosis in the apex of the lower lobe of the left lung. His

sputum contained tubercle bacilli. Artificial pneumothorax was instituted with satisfactory collapse. He was in government work and was treated in a federal institution. He was discharged in 1948 but continued to receive pneumothorax refills on an outpatient basis. He worked for one year.

In June 1949 he developed spontaneous pneumothorax on the right side while the left lung was still collapsed artifically. In 10 days after the spontaneous collapse, surgery was performed on the right side and the lung completely reexpanded. In August 1949 he developed pleurisy with effusion on the right side. Tubercle bacilli were recovered from fluid. He was again hospitalized for three months.

The left lung failed to re-expand when artificial pneumothorax was discontinued in January 1950. Decortication was done in May with complete expansion of the lung. Since that time his chest condition has remained satisfactory.

Occasionally in persons receiving artificial pneumothorax for tuberculosis, spontaneous pneumothorax occurs on the opposite side in the absence of any demonstrable disease in the lung or of mediastinal herniation as in the case just cited. This condition may occur at any time during treatment intervals.

In one case (not included in this study) who had been on artificial pneumothorax without complication over a considerable time spontaneous pneumothorax began to appear on the same side within an hour or so after refills. There was no likelihood that the lung had been punctured by the pneumothorax needle and it was assumed that a rent in the visceral pleura occurred at the attachment of an adhesion. At first one or two needle aspirations sufficed but finally this was not adequate and continuous aspiration became necessary for many hours. These attacks became so alarming that artificial pneumothorax was abandoned.

*Bilateral Pneumothorax.* Occasionally bilateral simple spontaneous pneumothorax is present when the first examination is made. This was found in one of our cases. This man of 28 years had this condition when his first symptoms occurred in November 1931. The right lung was completely collapsed and there was a pocket of air over the apex of the left lung. Both lungs re-expanded satisfactorily and no evidence of pulmonary disease could be found. (This case was reported by Dr. R. G. Hinckley, Journal-Lancet, 52:330, 1932.) This man had many bilateral recurrences during the next 20 years and died from malignancy in 1951.

Among persons who have recurrent simple spontaneous pneumothorax some have alternating attacks on the two sides and occasionally both lungs are found partially collapsed simultaneously. Bilateral collapse has occurred in nine of our 100 traced cases.

*Recurrence.* Brock has reported the largest and best presented series of cases of recurrent and chronic spontaneous pneumothorax from which he draws excellent conclusions from the standpoints of diagnosis and treatment.

We have kept in touch with or have recently traced 104 of our 115

cases. Only 100 are here considered as the remaining four had six months or less observation. In 71 of the 100 there has been no recurrence. The number of years since the initial episode is shown in *Table 6*.

TABLE 6
NO RECURRENCE

| No. Persons Traced | No. Years Since Attack | No. Persons Traced | No. Years Since Attack |
|---|---|---|---|
| 1 | 29 | 3 | 12 |
| 2 | 27 | 4 | 11 |
| 2 | 24 | 3 | 10 |
| 5 | 22 | 3 | 9 |
| 2 | 21 | 1 | 8 |
| 2 | 20 | 3 | 7 |
| 1 | 19 | 3 | 6 |
| 2 | 18 | 1 | 5 |
| 1 | 16 | 8 | 4 |
| 4 | 15 | 3 | 3 |
| 2 | 14 | 7 | 3 |
| 2 | 13 | 6 | 1 |

Seventeen have had one recurrence. However in five of them the second attack appeared within two months or less after the first, thus it is probable that the original rent reopened. In any event the 17 cases are shown in *Table 7* with the time intervals between the first and second

TABLE 7
RECURRENT SPONTANEOUS PNEUMOTHORAX
ONE RECURRENCE

| Same Side | Opposite Side | Interval Between First and Second | Time Since Last Attack | No. Years Since First Attack |
|---|---|---|---|---|
| | x | 21 years | 5½ years | 26½ |
| x | | 5 months | 20 years | 21 |
| x | | 9 years | 12 years | 21 |
| x | | 2 months | 15 years | 15 |
| x | | 1 yr. 9 mos. | 11 years | 13 |
| x | | 6 weeks | 10 years | 10 |
| x | | 3 years | 6 years | 9 |
| x | | 6 years | 3 years | 9 |
| x | | 1 yr. 9 mos. | 8 years | 9 |
| x | | 4½ years | 3 years | 8 |
| x | | 6 weeks | 7 years | 7 |
| x | | 2½ years | 3 years | 6 |
| | x | 4½ months | 4 years | 4 |
| x | | 2 months | 3 years | 3 |
| x | | 2 years | 1 year | 3 |
| x | | 6 weeks | 2 years | 2 |
| x | | 7 months | 11 months | 1½ |

attacks, between the last episode and the total time that has elapsed since the first attack. In 15 of these cases the second collapse occurred on the same side as the first.

Twelve have had more than one recurrence. The numerals in columns two and three, *Table 8*, indicate the number of attacks on the same or

TABLE 8
RECURRENT SPONTANEOUS PNEUMOTHORAX
TWO OR MORE RECURRENCES

| Same Side | Opposite Side | Interval Since Last Attack | Number Years Since First Attack |
|---|---|---|---|
| Many bilateral | | 6 years | 20 |
| Many bilateral | | Chronic | 16 |
| Numerous | | 6 years | 15 |
| Many bilateral | | 6 years | 13 |
| 5 | | 2 years | 13 |
| Many bilateral | | 9 years | 11 |
| 4 | 4 | 2 years | 10 |
| 3 | | 7 years | 9 |
| 4 | | 5 years | 8 |
| 2 | 1 | 4 years | 8 |
| 3 | | 1 year | 6 |
| 2 | 1 | 2 years | 6 |

the opposite side. All had recurrences on the same side and six also on the opposite side. Four with bilateral recurrences had so many attacks that they do not remember the number. On occasions both sides were partially collapsed simultaneously.

Two who have had many attacks on both sides never had bed rest for more than occasional brief intervals. They stated that they became accustomed to the condition and continued with their work. One had his last recognizable attack in 1947 and died from malignancy in 1951. The other has not had an attack during the past six years and is leading an active life.

A man of 39 years who began having frequent bilateral attacks in 1941 became so incapacitated that finally mild irritants were placed in the pleural cavities (lipiodol on one side and glucose solution on the other) to produce adhesions between the visceral and parietal layers of pleura. This was so effective that he has had no attack in the past nine years. However, he had a severe cardiac attack in 1952 which proved to be due to cor pulmonale.

A woman of 23 years had complete collapse of the right lung when first seen in 1937. No aspiration or surgery was done at that time. Later she was in another state where air was aspirated from time to time. In 1946 pneumonectomy was performed when a large cyst was found communicating with a bronchial ramification with a check valve. It was

not determined whether on previous occasions the cyst had ruptured into the pleural cavity or whether each collapse of the lung was due to pressure within the cyst. The latter seems probable. Since 1946 she has remained in reasonably good health.

A man of 21 years had an attack of spontaneous pneumothorax in November 1936. In subsequent years he had recurrences involving both sides. In 1944 in military service he was told that 10 per cent permanent pneumothorax was present at the apex of each lung. He was later discharged from service with a diagnosis of cystic disease. For several years he has resided in another state where his working capacity has been only slightly limited. The partial collapse of the apex of each lung has remained unchanged since 1949. It seems probable that his acute episodes were due to ruptured cysts and that the present apical conditions are due to the cysts themselves.

Treatment of recurrent simple spontaneous pneumothorax depends upon a number of factors such as frequency and severity of attacks. In our 100 traced cases 17 have had only one recurrence. Among the 12 who have had more than one recurrence eight have had more than three attacks. Apparently an attack of simple spontaneous pneumothorax usually does not result in symphysis of the pleurae. When spontaneous pneumothorax has recurred several times we have usually recommended procedures to prevent further attacks. In the earlier years of our work attempts were made to adhere the visceral and parietal layers of pleura by introducing into the pleural space 25 to 50 cc. of a mildly irritating substance, such as hypertonic glucose solution (30 to 60 per cent), lipiodol, or mineral oil. Brock[15] has found the production of pleurodesis by applications of silver nitrate the most satisfactory method he has employed. Recently we have recommended that chest surgeons explore and close rents in the pleura, remove pleural blebs in evidence and produce slight irritation of pleural surfaces by gentle friction with a sponge to insure pleurodesis.

### *Prevalence*

Our observations lead us to believe that simple spontaneous pneumothorax occurs far more frequently than the literature indicates. In discussing the subject with physicians it is not unusual to learn that many have seen from one to several cases which have not been reported. Occasionally persons are found to have this condition during examinations for other purposes without symptoms or other evidence of its presence. Some individuals with mild or moderate symptoms at onset do not report to physicians. A considerable number of our cases were not examined for from several days to more than a week after symptoms appeared. They probably would not have reported had symptoms been of shorter duration. Others are not diagnosed by their physicians but are treated for pleurisy, pneumonia, cardiac disease, etc.

The possibility of *previous attacks* having occurred among our cases was obtained from histories of symptoms. Two had spontaneous pneu-

mothorax definitely diagnosed on one occasion each (one patient—three years, another one year) before our first examination. Five stated that they had similar attacks of symptoms on from one to several occasions but never reported for examination before we saw them. It is not possible to be sure that they had spontaneous pneumothorax. However, one who had three such previous attacks described symptoms of shock on one occasion. On December 26, 1952 a nurse in our group wrote, "I have often thought that I probably had these attacks long before the diagnosis was made in 1939. While I was in training, 1925 to 1928, I had several attacks of so-called pleurisy. They were similar but less severe than later."

In five other cases attacks had occurred from a few months to five or six years before which they described as almost identical as far as symptoms were concerned. They reported to physicians and four were treated for pleurisy and one for pericarditis but no x-ray inspection of the chest was made.

*Prevention*

As yet no method has been devised to determine in whom this condition may occur since in most persons who have it x-ray inspection fails to reveal evidence of pleural blebs either before the attack or after the lung is re-expanded. In an occasional person who has not had an attack, however, pleural blebs or bullae may be sufficiently large to be detected on x-ray films. This does not necessarily indicate that such persons will have spontaneous pneumothorax. However, the potentiality might be reduced by removal of such blebs as can be found.

It is not known what causes blebs to rupture. We have seen persons who have had spontaneous pneumothorax onsets when engaged in most strenuous physical work and others while they were relaxed in sound sleep as well as those engaged in various intermediate degrees of activity. It appears that in some cases the visceral pleura becomes so thin or the pressure so high in the blebs that the increase in negative intrapleural pressure on quiet inspiration is adequate.

*Litigation* has frequently resulted from spontaneous pneumothorax. The person who is uninformed concerning this condition is likely to attribute sudden intense pain and dyspnea to his activity at the onset or to some strenuous work during the past few days. In such cases the physician is hard pressed to state with any certainty whatsoever that the condition would not have occurred even during sleep.

In persons who have had one or more attacks of spontaneous pneumothorax one should always issue a warning of the possibility of subsequent attacks and the advisability of prompt contact with the physician with the onset of symptoms. Even a minor degree of shortness of breath may indicate that a check valve is present and positive intrapleural pressure is developing. Delay can prove fatal in a short time. On a few occasions when the onset of recurrences have been reported on the telephone we have asked that no time be wasted in calling an ambulance but that a member of the family or an associate promptly rush the individual to the ambulance entrance of the nearest hospital. An intern or resident physician is called

and asked to be in readiness to aspirate air on the patient's arrival, if symptoms warrant. It is further requested that hospital authorities dispense with social service records, financial status, etc. until adequate treatment has been administered and the emergency has passed. In one of our cases who was promptly brought to a hospital by his wife on the appearance of the first symptoms, cyanosis and dyspnea were so extreme on arrival that the physician had to carry him from the automobile to the emergency room. The intrapleural pressure was so positive that when a needle was thrust through the chest wall there was momentarily a whistling of air rushing through the needle like that of a toy steam engine. Just as every physician is advised to have with him at all times tracheotomy equipment it is equally important that he always be prepared to promptly remove air in spontaneous pneumothorax emergencies.

Anyone who has had an attack of spontaneous pneumothorax should be advised against *high altitudes* especially in airplanes except in pressurized cabins and where oxygen can be administered. Persons recovering from spontaneous pneumothorax but in whom the lung is not completely expanded, no matter how small the mount of air still demonstrable, should also be warned against airplane travel except in pressurized cabins. The volume of air in a pleural cavity increases with altitude. Three thousand cc. in a pleural cavity at sea level assumes the volume of 3720 cc. a mile above. Therefore, a person with pneumothorax may be in distress at one mile and his life jeopardized at higher altitudes. At 18,000 feet the volume of air is doubled and at 34,000 feet, quadrupled.

Many physicians recall emergencies that were created early in World War II by transporting spontaneous pneumothorax cases by airplane. The problem was of such magnitude that in July 1944 the National Research Council issued an excellent special pamphlet prepared by J. J. Waring, Denver, Colorado on the diagnosis and management of spontaneous pneumothorax.[16] This was made available to our military medical officers everywhere.

## SUMMARY AND CONCLUSIONS

1. One hundred and fifteen cases of simple spontaneous pneumothorax are reported ranging in age from 15 to 64 years. Nearly one-half occurred between the ages 20 and 24 years. Eighty-five per cent of the entire group were males. The condition occurred on the left side only in 64, the right side only in 42 and bilaterally in nine.

2. In 78, initial symptoms were severe consisting mainly of pain and dyspnea. In the remainder the onset was gradual. Activities of the individuals when attacks occurred varied from strenuous work to sound sleep.

3. History of onset, physical signs and x-ray inspection were employed in diagnosis but fluoroscopy and x-ray films were most valuable.

4. Various degrees of collapse were observed. In 34 cases it was complete.

5. Approximately one third of these patients were treated ambulatorially while the remainder received bed rest, ranging from a few days to two months. Air was not aspirated except when positive intrapleural pressure developed. Thirty nine had small fluid accumulations which promptly dis-

appeared without aspiration. Only one presented a large effusion which was removed. The nine cases of spontaneous hemopneumothorax were aspirated until all evidence of blood disappeared.

6. Serious tension pneumothorax occurred in only two cases. Air was removed promptly and as long as positive pressure continued to develop. From two other cases, air was removed with the first manifestation of positive pressure.

7. Among the 115, there were 41 who had tuberculosis as manifested by the tuberculin reaction but no evidence of clinical disease was found. Two developed clinical tuberculosis five years after pneumothorax occurred. Another who did not react at the time of the initial pneumothorax developed clinical pulmonary tuberculosis 18 years later.

8. Contact has been maintained or recently re-established in 104 of the 115 patients. Four have been observed for six months or less. The remaining 100 have been observed from one to 29 years.

9. Among the 100 cases, 71 have had no repetition and 17 have had one recurrence all on the original side except two. Twelve have had more than one recurrence, ranging from two to many. In five of these, all recurrences were on the original side.

10. Since 29 of this group of 100 traced cases have had one or more recurrences, everyone who has had an initial attack should be advised of the possibility of others and how to proceed in the event symptoms of tension pneumothorax begin to appear.

11. From these observations and the management of recurrent spontaneous pneumothorax, the procedure now recommended after two or more attacks consists of surgical closure of the rent, removal of blebs in evidence and producing slight irritation of the pleural surfaces by gentle sponge friction.

12. In all initial attacks as well as recurrences, accumulations of fluid, large or small, should be removed if they do not absorb within a few days to avoid deposits of fibrin on the pleural surfaces.

13. In all cases of spontaneous hemopneumothorax, blood should be removed as often as necessary, transfusions administered when indicated and ligation of the vessel and closing the rent if copious bleeding persists unduly long.

14. Apparently simple spontaneous pneumothorax occurs more frequently than the literature indicates since not all physicians report their cases and many persons whose symptoms are mild do not consult physicians.

15. No method has been devised for the prevention of simple spontaneous pneumothorax but some recurrences can probably be prevented by surgical removal of blebs or producing symphysis of the pleurae.

16. Persons who have blebs or bullae demonstrated by x-ray inspection as well as those who have had one or more attacks of simple spontaneous pneumothorax, should avoid high altitudes except in pressurized cabins and where oxygen can be administered or a needle can be introduced into the pleural cavity in the event of emergency.

RESUMEN

1. Ciento quince casos de neumotórax espontáneo simple, se refieren con edades de 15 a 64 años. Casi la mitad, ocurrieron entre los 20 y los 24 años. Ochenta y cinco por ciento del grupo, eran del sexo masculino. La afección ocurrió en el lado izquierdo sólo en 64, en el lado derecho sólo en 42, y fué bilateral en nueve.

2. En 78, los síntomas iniciales fueron severos consistiendo en dolor y disnea principlmente. En los demás, el principio fué gradual. Las actividades de los individuos cuando el neumo principió fué variado, desde trabajo intenso, hasta el sueño profundo.

3. La historia clínica al principio, los signos físcios y la inspección a los rayos X, se emplearon para el diagnóstico, pero la fluoroscopía y la radiografía, fueron los medios más valiosos.

4. Varios grados de colapso se observaron. En 34 casos era completo.

5. Aproximadamente un tercio de estos enfermos, fué tratado ambulatoriamente, en tanto que el resto, se sujetó a reposo de pocos días, a dos meses. El aire no fué aspirado, sino cuando se encontraba presión positiva intrapleural. Treinta y nueve, tuvieron pequeño acúmulo de líquido que prontamente desapareció sin aspiración. Sólo uno, tuvo gran cantidad de líquido que requirió extracción.

Los nuve casos de hemoneumotórax espontáneo, fueron tratados por aspiración hasta que toda evidencia de sangre desapareció.

6. Sólo en dos casos se presentaron neumotórax espontáneos atensión. El aire se extrajo inmediatamente y tantas veces como se encontró prensión positiva. En otros dos casos se extrajo aire, tan pronto como hubo la primera manifestación de presión positiva.

7. Entre los 115, hubo 41 que tenían tuberculosis según la reacción tuberculínica, pero sin evidencias de la enfermedad clínica.

Dos, presentaron tuberculosis clínica cinco años después del neumotórax espontáneo. Otro, que no tuvo reacción tuberculínica cuandosufrió el neumotórax espontáneo, presentó tuberculosis clínica 18 años màs tarde.

2. Se ha mantenido el contacto o se ha re-establecido con 104 de los 115 casos.

Cuatro han sido observados por seis o menos meses. Los demás que son 100, se han observado de uno a 29 años.

9. Entre los 100, 71 no tuvieron reaparición y 17 han tenido una recurrencia, todos en el mismo lado, salvo uno. Doce tuvieron más de una recurrencia, desde dos a muchas. En cinco de estos, todas las recurrencias fueron del mismo lado.

10. Puesto que 29 de este grupo de 100, han tenido una o varias recurrencias, todo el que ha tenido un neumotórax espontáneo inicial, debe ser advertido de la posibilidad de otros accidentes semejantes y debe aconsejársele como proceder en el caso de que—aparezcan síntomas de tensión.

11. De estas observaciones y del tratamiento de los neumotórax espontáneos recurrentes, el procedimiento hoy recomendado después de dos o más ataques, consiste en la clausura quirúrgica delas fisuras, extirpación de las bulas, y la producción de irritación de la pleura por fricción suave.

12. En todos los ataques iniciales, así como en las recurrencias cuando hay acumulaciones de líquido grande o pequeño, debe ser extraído si no se absorbe dentro de pocos días, a fin de evitar depósitos de fibrina en la superficie pleural.

13. En todos los casos iniciales, así como en los recurrentes, la sangre debe extraerse tan a menudo como sea necesario; deben administrarse transfusiones cuando estén indicadas, ligadura del vaso, y cierre de la fisura, si la hemorragia persiste por tiempo—prolongado.

14. Aparentemente el neumotórax espontáneo simple, ocurremás frecuentemente de lo que indica la literatura, puesto que no todos los médicos relatan sus casos y muchas personas cuyos síntomas son moderados, no consultan a los médicos.

15. No se ha ideado método para prevenir el neumotórax espontáreo simple, pero algunas recurrencias pueden evitarse por la extirpación quirúrgica de los bulas a produciendo sínfisis de la pleura.

16. Las personas que tienen bulas o burbujas demostradas por los rayos X, así como los que han tenido uno o más ataques de neumotórax espontáneo simple, deben evitar altitudes elevadas, excepto en cabinas con presión compensada y en las que puede administrarse oxígeno a una aguja puede ser introducida dentro de la cavidad pleural en caso de emergencia.


## RESUME

1. L'auteur rapporte 115 cas de pneumothorax spontanés simples, s'étageant de l'âge de 15 à 64 ans. Environ la moitié des cas survinrent entre 20 et 24 ans. Dans 85% de cas, il s'agissait d'individus su sexe masculin. L'affection attint le côté gauche seulement chez 64 malades, le côté droit seulement chez 42, et la localisation fut bilatérale dans 9 cas.

2. Chez 78 malades, les symptômes de début furent sérieux, et consisterent essentiellement en douleurs et dyspnée. Pour les autres, il y eut des réactions variables Lorsque survint le pneumothorax, les malades avaient des activités très diverses, les uns se livraient à un travail de force, d'autres étaient plongés dans un sommeil profond.

3. L'histoire du malade, les signes physiques, et l'examen radiologique furent utilises pour le diagnostic, mais cel ui-ci fut avant tout basé sur la radioscopie et la radiographie.

4. L'auteur observa des degrés variables de collapsus. Dans 34 cas il s'agissait d'un collapsus complet.

5. Environ le tiers des malade put être traité de façon ambulatoire. Pour les autres, il fallut les aliter pendant une période oscillant de quelques jours à deux mois. L'auteur ne pratiqua pas de désinsufflations sauf lorsqu'il a existé une pression intrapleurale positive. 39 malades eurent en petit épanchement liquidien, qui disparut rapidement sans ponction. Un seul d'entre eux en un épanchement important qui dû être évacué. Les neuf cas d'hémopneumothorax spontanés furent ponctionnés jusqu'à ce que toute trace de sang ait disparu.

6. Dans deux cas seulement, il y eut un pneumothorax grave à pression positive. Il fut rapidement désinsufflé, et on continua les désinsufflations

tant que la pression resta positive. Dans deux autres cas, dès que l'on s'aperçut que la pression était positive, on pratiqua une aspiration.

7. Parmi les 115 malades, il y en eut 41 dont la réaction tuberculinique était positive, mais sans qu'aucune manifestation tuberculeuse put être mise en évidence. Deux d'entre eux furent atteints de tuberculose pulmonaire clinique cinq ans après leur pneumothorax. L'un d'entre eux qui ne réagit pas à la tuberculine lors de son premier pneumothorax fit une tuberculose pulmonaire clinique 18 ans après.

8. L'auteur a pu se maintenir en relation ou reprendre un contact récent avec 104 de ses 115 malades. Quatre d'entre eux ont été observés six mois au moins. Les cent autres ont été mis en observation de I à 29 ans.

9. Parmi les 100 malades, 71 ne firent pas de nouveaux pneumothorax, et 17 eurent une récidive toujours, saus chez deux d'entre eux, du côté où avait eu lieu la première localisation. 12 eurent plus d'une récidive. Chez cinq d'entre eux, toutes les récidives eurent lieu sur le côté primitivement atteint.

10. Du moment que 29 parmi les cent malades atteints ont eu une ou plusieurs récidives, il faut que tout individu qui a été atteint d'un pneumothorax spontané soit informé de la possibilité de nouvelles attaques, et qu'il sache comment faire si des symptômes de pneumothorax hypertensif apparaissent.

11. En partant de ces observations et du comportement des pneumothorax spontané récidivants, l'auteur recommande maintenant dans les cas d'attaques répétées deux fois ou davantage, de pratiquer la fermeture chirurgicale de la plaie pulmonaire, la suppression des bulles perceptibles, et la production d'une petite irritation pleurale par friction à l'aide d'une éponge mousse.

12. Dans tous les cas de première attaque, aussi bien que lors de récidives, les épanchements liquidiens abondants ou non doivent être évacués s'ils ne se résorbent pas en quelques jours. On évite ainsi les dépôts fibrineux sur la surface pleurale.

13. Dans tous les cas d'hémopneumothorax spontanés, le sang doit être retiré aussi souvent qu'il est nécessaire, des transfusions doivent être faites si elles sont indiquées, et si une hémorragie abondante persiste d'une façon anormalement prolongée, il faudra pratiquer la ligature du vaisseau et la fermeture de la plaie pulmonaire.

14. Il semble que les simples pneumothorax spontanés surviennent plus fréquemment qu'ils ne sont indiqués dans la littérature médicale, étant donné que tous les médecins ne publient pas leurs cas, et que de nombreux individus dont les symptômes sont très modérés ne consultent pas leur médecin.

15. L'auteur n'envisage pas une méthode de prévention du simple pneumothorax spontané mais il semble que certaines récidives puissent être vraisemblablement évitées grâce à l'extirpation chirurgicale des vésicules ou grâce à la production d'une symphyse pleurale.

16. Les individus chez lesquels l'examen radiologique a mis en évidence des vésicules pulmonaires ou des kystes aériques, et ceux qui presentent une ou plusieurs fois un pneumothorax spontané semblent devoir éviter de

se soumettre aux hautes altitudes, sauf dans des cabines "pressurisées" et ou l'on peut administrer de l'oxygène. Il faut également qu'une aiguille puisse être introduite dans leur plèvre en cas de danger.

## REFERENCES


1 Riolan, J.: "Encheiridium Anatomicum et Pathologicum," *Parisiis, G. Meturas*, 1648.
2 Littre, A.: *Mem. de l'Acad. des Ac.*, p. 10, 1713.
3 Meckel: "Sur de l'air repandu remasse dans la cavite du thorax qui arretait la respiration et qui a cause la mort," *Mem. de l'Acad. Roy. de Ac. de Berlin*, 15:—, 1759.
4 Itard, J. E.: "Dissertation sur le pneumothorax ou les congestions gaseuses qui se forment dans la poitrine," *Thesis, Paris*, 1803.
5 Laennec R. T.: *De l'auscultation mediate*, 1819.
6 Emerson, C. P.: "Pneumothorax," *Johns Hopkins Hospital Reports*, 11:1-450, 1903.
7 Hewson, W.: "The Operation of the Paracentesis Thoracis Proposed for Air in the Chest: With Some Remarks on the Emphysema, and on Wounds of the Lungs," *General Med. Observation and Inquiries*, vol. 3. Read June 15, 1767.
8 Biach, A.: "Sur aetiologie du pneumothorax," *Wien. med. Wchnschr.*, 30:—, 1880.
9 Palmer, J. P. and Taft, R. B.: "Spontaneous pneumothorax," *J.A.M.A.* 96:653, 1931.
10 Weber, F. P.: "Pneumothorax in Tuberculous Subjects," *Lancet*, 2:813, 1905.
11 Barlow, N. and Thompson, J. C.: "Small Pneumothorax in Tuberculosis," *Hygienic Lab. Bull.*, no. 132, Sept. 1922, Washington Government Printing Office.
12 Kjaergaard, H.: "Spontanous Pneumothorax in the Apparently Healthy," *Copenhagen*, 1932. Levine and Munksgaard.
12a Kjaergaard, H.: "Pneumothorax Simplex," *Acta Med. Scand.*, 80:93, 1933.
13 Hamman, L.: "Spontaneous Interstitial Emphysema of the Lungs," *Tr. A. Am. Physicians*, 52:311, 1937.
14 Leggett, E. A., Myers, J. A. and Levine, I.: "Spontaneous Pneumothorax, A Report of 31 Cases," *Am. Rev. Tubere.*, 29:348, 1934.
14a Rugi, C.: "Pneumothorax bei einem Neugebrenan Ztsch. F. Gebutsch," *U. Gynak*, 2:31, 1878.
15 Brock, R. C.: "Recurrent and Chronic Spontaneous Pneumothorax," *Thorax*, 3:88, 1948.
16 Waring, J. J.: "Spontaneous Pneumothorax," *Office of Medical Information, National Research Council*, Washington, D. C., 1944.

# Pulmonary Resection in Childhood Tuberculosis

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The indications for surgery in childhood tuberculosis differ from those in adults because of the basically different anatomical lesions produced in primary disease. In the main, excision is only indicated when endobronchial disease results in collapse and fibrosis of the lobe involved, or in bronchiectasis. Tuberculomata are occasionally present, and pose the problem of round shadows in the chest. Thoracotomy is sometimes necessary to establish the correct diagnosis and they are then removed. In those cases in which correct diagnosis can be established without exploration, there seems little indication for operation as their natural history is usually one of harmless regression. It is therefore incumbent upon us to discuss, at least briefly, tuberculous bronchitis and bronchial obstruction before discussing surgery in tuberculosis.

In the past 24 years, since the first pulmonary resection for any cause was done at the Hospital for Sick Children, Toronto, 250 such operations have been done. Eight per cent of these were necessitated by tuberculous disease. This is only slightly less than the 10 per cent due to disease produced by foreign bodies. During this same period, but with much greater frequency in the past six years, 250 bronchoscopic studies have been made on 94 tuberculous children. Bronchograms were made in 75 of these cases. The bronchoscopic examinations were all made under general anesthesia, and the radio-opaque substance was injected through a catheter in the bronchoscope into the diseased area. The visualization under anesthesia allows more careful, as less hurried, examination. Excess of granulations or caseous material could be removed not only for therapeutic reasons but to permit a better bronchogram. A detailed report of these studies will appear elsewhere but the salient points must be given here to appreciate the problem of excisions.

Seventeen of the children presented no symptoms or bronchographic evidence of endobronchial disease. They were studied to establish a base line in tuberculous children so that deviations from normal could be better appreciated. This leaves 77 children who gave demonstrable evidence by bronchoscopic examination and bronchography of pathological lesions in their bronchial trees and its resultant effects on their lungs. Most of them had suggestive symptoms, but a few did not. In addition autopsy material was studied for evidences of bronchial lesions and bronchiectasis of tuberculous origin. Four of these had been treated for two to four months with streptomycin for tuberculous meningitis which did not respond. These presented bronchial lesions plus bronchiectasis. Such well

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established disease of this type was uncommon before the streptomycin era. The child with such severe infection usually died from overwhelming tuberculosis before its establishment.

Two types of endobronchial tuberculosis were observed to develop in primary tuberculosis. They present distinct differences and possibly variations in their response to drugs and thereby in their indications for surgery. They are: (1) Bronchiectasis produced by the rupture of a contiguous gland, or glands, into the bronchus with resultant injury to the bronchial wall, and obstruction; (2) Primary infection of the bronchial mucosa with tuberculosis. This may be due to lymphatic spread or be a hematogenous or an implantation infection. The first of these presents a picture of sessile granulations protruding from a bronchus. These may grow so large as to occlude a bronchus and demand urgent removal, or recur so rapidly that bronchoscopic removal is frequently necessitated. Much caseous material can usually be sucked out of the affected bronchus. Later ulcers and subsequent strictures at the points of rupture cause irregularities and constriction of the bronchus. Daley[1] considers this the most frequent type of endobronchial disease. This type of lesion has been present in all our lower lobe cases, but may also involve upper or middle lobes. Should a secondary bacterial infection occur, ordinary purulent bronchiectasis may develop along with the tuberculous lesions. The second type presents a less dramatic picture through the scope. At first little other than redness and swelling with a little greyish secretion is seen. Later, ulcers occur but no granulations protrude and caseous material is largely lacking. If allowed to run its course, this type may proceed to fibrosis and stricture of the bronchus with concommitant collapse of the airless lobes, or proceed to the development of typical tuberculous bronchiectasis. This is characterized by proximal ectasia with distal normal sized bronchi, surrounded by emphysematous lung. The bronchogram shows alveolarization of the peripheral portion of the parenchyma. Tubercles may be present in the parenchyma and persist for years and whose potentialities for reinfection no one knows. Upper or middle lobe bronchi are most often involved.

The association of congenital anomalies with tuberculous bronchiectasis in this small series merits mention for two reasons. Some observers, such as Baum[2] consider tuberculous bronchiectasis is frequently superimposed on previous non-tuberculous disease. Secondly, pulmonary sequestration is not usually associated with tuberculosis. Two of ours (cases 11 and 14) had sequestrated masses with systemic blood supply in their lower right chests. These masses were filled with caseous material and tubercle bacilli, and the contiguous lobes presented ordinary tuberculous bronchiectasis. Three other cases (numbers 4, 9 and 13) had a tracheal origin of their right upper lobe bronchus. One of these (13) had a completely separate pleural cavity for the upper lobe and a vascular supply from the subclavian. This lobe presented a constrictive tuberculous bronchiectasis, while the lower and middle lobes showed saccular disease. Thus five of our tuberculous resections had congenital lesions. Only eight of the 230 non-tuberculous cases did.

Table I

| CASE | X-RAY | BRONCHOSCOPIC | BRONCHOGRAM |
|---|---|---|---|
| 1.A.A | Δ Shadow rt. base with superimposed cystic shadow | Much tuberculous granulation tissue and caseous material rt. main bronchus | Rt. middle lobe collapsed and lying along mediastinum-appear cystic. Bronchi do not fill well because of obstruction with caseous tissues. |
| 2.R.W | Δ Basilar shadow rt. chest. | No ulcer. No caseous material. No apparent obstruction. Grey mucoid secretion. | Bronchiectasis dorsal segment of rt. lower lobe. |
| 3.L.C | Δ Non-homogenous shadow rt. base | Granuloma rt. main bronchus, consisted of caseous necrotic material. | Tuberculous bronchiectasis rt. lower lobe with big dilatations. Constricted rt. middle lobe with T.B. bronchiectasis. |
| 4.R.A | Collapsed rt. upper. Diffuse shadow with some necrotic areas rest of lung | Rt. upper lobe bronchus off trachea. Caseous material main rt. bronchus. | Abnormal origin rt. upper lobe bronchus. Constrictive T.B bronchiectasis upper lobe. Widespread marked bronchiectasis rt. middle and lower. |
| 5.J.M | Shrunken rt. middle lobe. | Rt. main bronchus full of caseous material - removed by forceps. Recurred quickly. | Collapsed lobe. Compressed bronchi - irregularity of bronchial walls. |
| 6.G.G. | Shrunken rt. middle lobe. | Constriction rt. middle lobe bronchus. Grayish mucoid secretion. | Atelectatic and fibrosed rt. middle lobe, Constriction of main bronchus. |
| 7.L.Y. | Homogenous shadow whole lower rt. chest | Granular carina. Bronchus to rt. middle and lower lobe filled with cheesy material. | Bronchiectasis rt. lower lobe. |
| 8.S.M. | Homogenous shadow left upper lobe. | Left upper bronchus red and bleeds easily | Collapsed left upper lobe with dilated pectoral bronchus. |
| 9.T.M. | Homogenous shadow rt. upper - smaller than normal. | Rt. upper bronchus red and constricted. Origin from trachea. Mucoid secretion. | Constricted collapsed bronchi. Rt. upper lobe bronchus arises from trachea. |
| 10.L.M. | Collapsed lower left lobe probably also lingula. | Bronchus to left lower lobe constricted. Mucopurulent secretion. | Dilated lingula bronchus cavity left lower. Constriction of bronchi. Collapse parenchyma. |
| 11.R.A | Large solid shadow, rt. lower chest. No med. shift. | Rt. main bronchus obstructed with pus, caseous material and many granulations. | Bronchiectasis rt. lower lobe. Filling defect below this. |
| 12.J.C. | Homogenous opaque rt. middle lobe. | Bronchial mucosa rt. middle lobe Bronchus hemorrhagic. Greyish mucoid secretion. | Bronchectasis rt. middle lobe. |
| 13.L.M | Opaque shadow, small-rt. upper lobe. | Slight injection rt. upper lobe bronchus. No granulations | Tracheal origin rt. upper lobe bronchus. Collapsed parenchyma. Constricted bronchi. |
| 14.A.B. | Dense homogenous shadow rt. lower chest No med. shift. | Cheesy caseous material rt. lower lobe bronchus. Pus when this cleared. | Bronchiectasis rt. lower lobe. Filling defect after normal bronchi filled with lipiodol. |
| 15.O.P. | Diffuse shadow inner 2/3 of whole left chest. Aerated areas. | Bronchial constriction left upper lobe. Granulation left lower lobe bronchus. Pus and caseous material | Constriction upper lobe bronchus with dilatation or cavities beyond T.B. bronchiectasis remainder left lung. |
| 16.H.B. | Heavy streaking from hilus left lung. Some areas of collapse. | Left lower lobe bronchus granulations. Pus and greyish mucoid material | Left lower lobe and lingular bronchiectasis. |
| 17.H.K. | Rt. upper lobe-small, collapsed, solid. | Constriction and small ulcer rt. upper lobe bronchus. | Constriction rt. upper lobe bronchus. Proximal dilatation of bronchi. Collapsed lung. |

Before proceeding to the indications for surgery, some attention should be directed to the possibilities that less drastic treatment of tuberculous bronchiectasis would be effective. Before surgery of the chest became so

good, bronchoscopic suctions in purulent bronchiectasis seemed invaluable. Their use even caused reversion of the ectasia when used in acute cases. When streptomycin became available, it appeared to us that this drug plus bronchoscopic suctions might cure tuberculous bronchial lesions. On the whole, the results were disappointing. Ten of the patients thus treated were little influenced by this therapy and had excisions. The four post mortem cases showed marked bronchiectasis with parenchymal tuberculosis. Only one of the cases treated thus was resistant to streptomycin (case 15). Two showed many tubercles in the parenchyma of the resected specimen. One case (5) showed no tubercles but positive cultures and guinea pigs were obtained from the lung tissues. These findings were found not only in the acute cases but were seen in one resected two, and one three years after acute disease had subsided. These facts, plus the fact that ten others of these cases so treated have not only shown persistent lesions but have developed symptoms that now make resection advisable, show that streptomycin, or this plus PAS and repeated suctions, is often ineffectual in curing disease but leaves behind silent disease which will cause future trouble.

The combination of suctions and isoniazid looks more promising. None of these cases have had resections yet so there is no pathological proof. In nearly all of them the clinical and bronchoscopic findings suggest a greater degree of healing has occurred. In three bad cases, the bronchiectasis as depicted by the bronchogram has been reversed. Possibly the superiority of isonicotinic acid compounds in penetrating both caseous masses and intracellular organisms accounts for this better response.

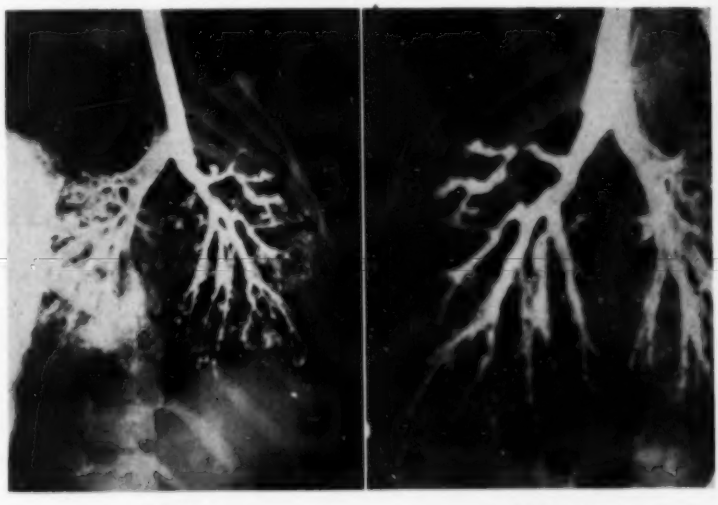

FIGURE 1 FIGURE 2

*Figure 1*, (Case 15)—Bronchogram. Note constrictive lesion left upper lobe bronchus. *Figure 2*: In lower lobe observe the proximal dilatations of the bronchi with peripheral narrowing and alveolarization of the lipiodol. Bronchiectasis secondary to caseous glands.

## Table II

| CASE | AGE | ACUTE or CHRONIC | THERAPY | RESECTED | SPECIMEN | Tbc. SPECIMEN |
|---|---|---|---|---|---|---|
| 1 A A | 2 yrs. | Subacute | Bronchoscopics Streptomycin | Rt middle and lower lobes. | Lower lobe very firm. Nodular consolidation rt. middle. Caseating glands about main bronchus, principally rt., middle. Gross bronchiectasis in lower lobe. Tubercles. | G.P. neg Culture.. neg |
| 2 R W | 10yrs | Chronic | Rest in bed. | Rt. lower lobe | Markedly shrunken. Gen. bronchiectasis. No T.B. | Neg. |
| 3 L C | 4 yrs. | Subacute | Bronchoscopics Streptomycin | Rt lower and middle lobe. | Bronchiectasis lower T.B. in type. Shrunken middle lobe - proximal dilatations. | Neg. |
| 4 R A | 10 yrs | Subacute | Streptomycin Bed rest 2yrs. | Pneumonectomy (rt. lung) | Rt. upper shrunken and distorted. Bronchus from high in trachea Sep. pleural cavity Gross bronchiectasis caseous areas rt. lower and middle Tubercles. | + Culture + G.P. |
| 5 J M | 14mos. | Acute | Streptomycin | Rt. middle lobe | Middle lobe collapsed. Bronchioles dilated. Parenchyma reduced and many tubercles. Much caseous material. | G.P. neg. Cult. neg. |
| 6 G G | 8 yrs. | Chronic | None | Rt. middle lobe | Much fibrosis. Bronchi mod. dilated - close together. No tubercles | G.P neg |
| 7 L Y | 7 yrs. | Subacute | Streptomycin + suctions. | Rt. lower lobe | Rt. lower collapsed and hidden. Diffuse thin walled dilated bronchiectasis. Tubercles. | Cult. neg G.P. + |
| 8 S M | 2½ yrs. | Subacute | Streptomycin I.P.A.S. suction | Rt. upper lobe | Some collapse of lobe. No tubercles. Pectoral bronchus dilated into cavity. | Cult. + G.P. + |
| 9 T M | 5 yrs. | Chronic | 4 yrs. in another san. Some streptomycin. | Rt. upper lobe | Cavity rt. upper was caseous necrosis. Constricted collapsed bronchi Tracheal origin bronchus. | + G.P. neg. cult. |
| 10 L M | 14yrs. | Chronic | Bedrest. No chemotherapy | Left lower and lingula | Lingula collapsed bronchi. Generalized dilatation lower lobe. Tubercles | Neg |
| 11 R A | 5 yrs. | Acute | Bronchoscopic suctions | Rt. lower Sequestrated lobe | Bronchiectasis rt. middle with caseous areas. Sequestrated lobe full of cysts with caseous material. | G.P. + |
| 12 J C | 9 yrs. | Chronic | Suctions | Rt. middle lobe | Caseous glands Collapsed middle lobe All bronchi show ectasia. | G.P. + |
| 13 L M | 4 yrs. | Chronic | Chiefly bed rest. A little streptomycin | Rt. upper lobe. | Shrunken lobe Constricted and collapsed bronchi. No tubercles. Tracheal bronchus. | Neg |
| 14 A B | 5 yrs. | Acute | Suctions | Rt. lower and mass | Sequestrated mass. Lower lobe bronchiectasis. Caseous areas. | +G.P. |
| 15 O P | 4 yrs. | Acute | Streptomycin PAS Viomycin chloromycetin (Resist. to all but last.) | Left lung | Multiloculated cavities - upper lobe beyond constricted bronchus. Bronchiectasis (proximal) both lobes. Caseation tip of lingula | + Cult. + G.P. |
| 16 H B | 11 yrs. | Chronic | None | Left lower and lingula | Healthy parenchyma Irregular bronchiectasis and increased lymphoid tissue. Lower bronchus granulomatous. | |
| 17 H K | 17mos. | Acute | Streptomycin P.A.S. | Rt upper | Nodules (caseous) in periphery. Branchi distended. Many tubercles focal necrosis. | Cult. + G.P neg. |

It is good practice before suggesting major surgery, to consider the balance between the risk of such a procedure and the possible complications it entails. Children are well known to stand lobectomies and pneu-

monectomies well. The younger they are, the better they are immediately after operation and their functional recovery is good. The tuberculous children who have had resections have made an even more rapid recovery from operation than ordinary bronchiectatics. There has been no mortality, operative or post-operative. No post-operative complications have developed since the use of streptomycin before and after surgery. The first resection for tuberculous disease, done in 1930, developed contralateral tuberculous disease from which he eventually recovered. One patient (case 15) developed tuberculous pericarditis one year after pneumonectomy. Two observers, Bérard[3] and Murphy[4] have recently described this as a complication of resection. In our case the cardiac involvement occurred a year after resection following an acute infection. More cases of tuberculous pericarditis are presenting since more severe disease is treated, and our feeling is that this case developed her disease as a result of infection from adjacent glands as did the four others recently seen and had nothing to do with the operation. After a year, it is apparently cured with rest and isoniazid. We feel we are right in assuming that pulmonary resections for tuberculous bronchiectasis in children offer at most a minimal risk of mortality and morbidity. No late complications have appeared in the two to four year period. The children appear in excellent health and present good pulmonary function.

The optimal time at which surgery should be performed poses the next question. From 1946 to 1952, it was our practice to give a course of streptomycin for four to six months, with bronchial suctions as needed. Further rest was given for four to six months and then excision done if healing had not occurred. Latterly, being less impressed by the possibility of cures without excision, it seemed highly desirable that this should be done earlier when the patient's organisms were still sensitive to streptomycin. Operations have therefore been carried out just as soon as the disease elsewhere became stabilized. This has usually been in four to eight months. In one case (case 8), on opening the chest it was felt that too much active disease prevailed around the lobe to proceed with excision and the chest was closed. The resection was done four months later. This speeding up of the time of operation has not only taken advantage of aid from drugs while they are still effective but has shortened the length of time in hospital. This has, of course, only been applied in those cases in which surgery was apparently inevitable.

It has been felt that those cases showing improvement should be left for a period before resorting to surgery. It is a moot question now, whether those presenting with a collapsed fibrotic lobe and no symptoms should ever be operated upon. Opinions differ as to potential dangers of fibrotic shrunken lobes or even asymptomatic bronchiectasis, as these possibly represent only inactive healed sequelae of active tuberculosis. Magnin[5] states unequivocably that they should be left alone. Others consider them as hidden tuberculosis. James[6] and his coworkers reviewed cases at a mean average of three and one half years later and conclude from their bronchograms that this damage to the bronchi is permanent.

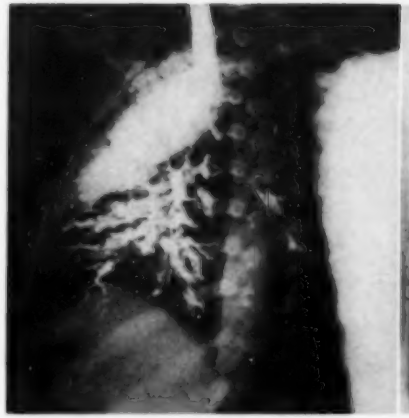

FIGURE 3

FIGURE 4

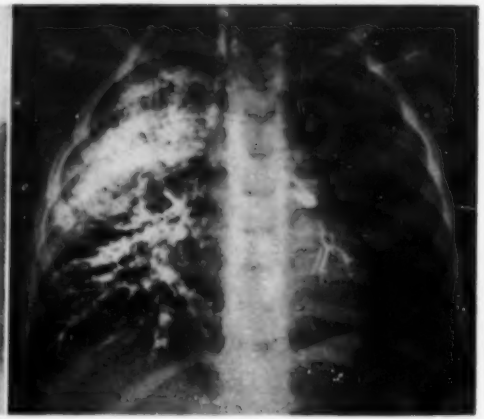

FIGURE 5

*Figure 3*, (Case 3)—Bronchogram and specimen. Again note proximal dilatation and peripheral narrowing. Peripheral alveolarization. *Figure 4*: Specimen—right lower and middle lobes. Note many depressions in main bronchus where caseous glands have perforated. *Figure 5*: Bronchiectasis secondary to caseous glands.

This was of course without benefit of suitable drugs. Veneckles[7] has reported marked residual changes after one to sixteen years. Rogstad[8] has shown that cultures may remain positive for years despite calcification of adjacent tissues. In four of the five cases of this small group not resected for two to four years, two still had active tubercles in the resected specimen. One of these had been streptomycin treated, and one had not.

Our inclination at present would be to do more cases earlier. This not only permits operation while the drug is effective and shortens the stay in hospital, but obviates a long period of anxiety and watchfulness. Otherwise later admission for excision often becomes necessary. This is true in 10 of our cases already. The only exception would be to permit a longer period of observation of those patients now being treated with isoniazid. This would permit one to see if the promise of progress with this drug will be maintained.

The need for operation may be discussed in two groups of patients, the acute and the subacute or chronic. The indications are listed below:

I *Acute Cases*

1. Persistent positive sputa from the involved area after a course of treatment.
2. Persistent cough or localized "wheezing."
3. Bronchoscopic evidence that ulcers are not healing and the disease progressing.
4. Bronchographic evidence of bronchial irregularity, constriction or bronchiectasis that shows no sign of regressing.
5. Persistent constrictive collapse of a lobe.
6. Added purulent infection in the bronchiectatic area.
7. Radiographic evidence of massive lower lobe involvement.
8. The presence of an associated congenital lesion.

II *Subacute or Chronic Cases*

1. Pneumonic episodes involving the diseased area.
2. Recurrence of positive sputum not accounted for by other lesions.
3. Failure to reverse the ectasia.
4. Secondary non specific bronchiectasis.
5. Poor general health indicating a secret focus of infection.

Time and more cases will tell what proportion of residual fibrosed and shrunken lobes, without symptoms, possess inherent infective qualities years later.

The contraindications to operation would appear to be extensive bilateral disease, and at least serious consideration before operating on those whose organism is completely insensitive to antibacterial drugs. One such case was done in our series. The secretions, both purulent and tuberculous, were so great from the totally diseased left lung that death appeared likely. Pneumonectomy was performed although there were cavities on the right side. The operation preserved her life without too much progress toward health until a year later when isoniazid came to her rescue as the first drug her organism was sensitive to, and with its help both her pulmonary disease and subsequent pericarditis are apparently healed.

The results of resection in this series of cases have been excellent. The two cases done in 1930 and 1931 with accompanying sequestration are in good health. The first of these had subsequently, 10 years later, to have his right upper and middle lobes removed for bronchiectasis. The other returned in 1952 for a follow up being done on all the cases of pulmonary excision. He was well and had good pulmonary function. A parodoxical movement of his right diaphragm from the phrenicotomy done preoperatively still persists. The one done in 1935 has been well ever since. The ones done since streptomycin was available have been perfectly well in the two to four years since the excision was done. None of them have had any evidence of recativation or reinfection tuberculosis.

## SUMMARY

A brief review of endobronchial tuberculosis is given as its incomplete healing will provide most of the cases needing resection in childhood. The operative mortality is low and the end results good. Resection is indicated when permanent damage ensues after endobronchial tuberculosis in both acute and chronic cases. In the former, the persistence of positive sputa from the diseased area, persistent cough or "wheezing," and when bronchoscopic evidence shows lack of healing and bronchiectasis indicate

FIGURE 6, (Case 7): Rt. lower lobe. Again note dilations are proximal. Massive and miliary invasion of lobe with tubercules. Lung removed 1½ years after initial acute infection.

operation. Secondary infection in the diseased area makes operation imperative. In chronic disease, pneumonic episodes involving the collapsed area, recurrence of positive sputum, failure to reverse the ectasia and poor general health indicative of hidden infection warrant removal of the affected area.


## RESUMEN

Se hace una breve revista de la tuberculosis endobronquial,—puesto que su curación incompleta provecrá de la mayoría de los casos que en la infancia necesitan resección. La mortalidad operatoria es baja y los resultados finales son buenos. La resección está indicada cuando después de tuberculosis endobronquial hay daño permanente tanto en los casos agudos como en los crónicos. En los primeros, la persistencia de esputos positivos provinientes del áreaenferma, tos persistente o "silbido" o cuando la broncoscopía demuestra la falta de curación y bronquiectasis, está indicada la operación. La infección secundaria del área enferma, hace la operacion indispensable. En los casos crónicos, los episodios neumónicos comprometiendo el área colapsada, la recurrencia de los esputos positivos, la falta dereversión de la ectasia y el mal estado generalque indica infección oculta, justifican la resección de la parteafectada.

## RESUME

L'auteur fait une revue rapide de la tuberculose endobronchique. Dans la plupart des cas, c'est la résection qui mettra fin, chez l'enfant, aux séquelles consécutives à une guérison incomplète. La mortalité opératoire est peu élevée, et les résultats satisfaisants. La résection est indiquée dans les cas chroniques comme dans les cas aigus, lorsque la tuberculose bronchique entraine des lésions irréversibles. Dans les cas aigus, la persistance de germes provenant de la région atteinte, la toux persistante ou le "wheezing," la bronchoscopie montrant l'absence de guérison et l'existence de dlatations bronchiques sont des indications d'opérer. Une infection secondaire de la zone atteinte rend l'opération indispensable.

Dans les formes chroniques, il y a une indication formelle de pratiquer l'exérèse de la région atteinte lorsque surviennent des épisodes pneumoniques intéressnt la zone atélectasi que. La réapparition de bacilles de Koch dans l'expectoration, l'échec du traitement contre la bronchectasie et la déficience de l'état général, témoin d'une infection latente.


## REFERENCES


1 Daley, J. F., Brown, D. S., Lincoln, Edith and Wilking, V.: "Endobronchial Tuberculosis in Children," *Dis. Chest*, 22:380, 1952.

2 Baum, O. and Amberson, J. M.: "Non-tuberculous infections complicating pulmonary tuberculosis," *Am. Rev. of Tubere.*, 45:243, 1952.

3 Bérard, M., Jacquanet, L. R. and Arribibaut, R.: "Les péricardites après exérèsis pulmonaire pour tuberculose Poumon," 8:6929, 1952.

4 Murphy, J. D. and Becker, B.: "Intermediary Report of 102 Streptomycin protected Pulmonary Resectons," *Am. Rev. of Tubere.*, 67:22, 1953.

5 Magnin, F., Fecon, J. L.: "Rapport entre les bronchiectasies et les lesions pulmonaire de le tuberculose tertiare Hanish & Feraldi," *Rev. de la tubere.*, 15:245, 1951.

6 James, E. M., Peck, W. M. and Willis, H. S.: "Bronchiectasis following primary tuberculosis," *Am. Jour. Dis. Ch.*, 72:296, 1946.

7 Veneckles, G. M.: "De Mögelijke Gavolgen von Primaire Longtuberculosa voor de Bronchi," *Nederl. tidschr. v. geneak*, 95:1295, 1951.

8 Rogstad, K.: "Lymphadenitis tuberculose bronchostenotic," *Acta tubere. Scandinav.*, 25:305, 1951.

# Sarcoidosis: Some Concepts of Etiology and Diagnosis*

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Though the etiology of sarcoidosis is unknown, the considerable information concerning it warrants discussion for what light it might shed. Since it has been assumed by many investigators that sarcoidosis is a disease of infectious etiology, most etiologic studies have centered around attempts at isolation of infective agents. Bacteria of a wide variety have been incriminated, but no successful and reproducible isolations are recorded. Similarly, the occasionally reported isolation of viruses has not been confirmed. Cultural and tissue-staining techniques have, at times, lent some weight to the idea that fungi might cause sarcoidosis, but such studies also lack confirmation. The recent suggestion that certain histologic features resembled lesions produced by nematodes is interesting, but unconvincing.[1] The negative results of such isolation studies recorded above by no means rule out the infectious nature of sarcoidosis. One need only recall the complete lack of fruitful studies in the 1918 influenza epidemic, presumably because the proper animal and the appropriate route of inoculation were not used.

Most of the investigation and controversy has centered around the relationship of sarcoidosis to tuberculosis and the possible role of the tubercle bacillus in its etiology. Early studies revealed certain pathologic similarities between the "hard" tubercle of sarcoidosis and the "soft" tubercle of tuberculosis. The rarely reported isolation of tubercle bacilli from either lesions or sputum has evoked considerable interest along these lines. However, many competent investigators have had consistently negative results. That there is a higher incidence of eventuation into, or development of, tuberculosis in patients with sarcoidosis seems apparent from results of many series. However, it should be noted that there is a tremendous spread of the figures. For example, Riley[2] has recorded that 25 per cent of his patients ultimately developed tuberculosis; whereas, of 25 patients observed at the Massachusetts General Hospital from 5 to 28 years, none has developed tuberculosis.[3] The discrepancies are difficult to reconcile. If there is a higher incidence of tuberculosis, it would appear that two explanations might be offered: 1) that many patients have spent some time on tuberculosis wards and have had an opportunity for heavy exposure; or 2) sarcoidosis in the lungs might behave as do other pulmonary diseases and "lower local resistance" to tuberculosis. Silicosis is an example of such a disease. The concept of "positive anergy" has been advanced to explain the relationship with

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tuberculosis.[4] According to this thesis, the frequently occurring negative tuberculin reaction is a result of the patient's excessive immunity to tuberculosis. As a result of this, he rapidly destroys the tubercle bacillus and has such a high degree of immunity that the tuberculin reaction is negative. The resulting histologic "sarcoid" picture is then ascribed as that of a person highly immune to tuberculosis. Such would, indeed, be a unique immunologic phenomenon.

If one examines the negative evidence concerning the relationship with tuberculosis, one immediately begins with the tuberculin reaction. A negative reaction in approximately 65 per cent of the cases indicates that the tubercle bacillus plays no role in the causation of sarcoidosis; for, indeed, such a record of cutaneous sensitivity would represent a rather unique immunologic situation. Recent studies have indicated that the high incidence of the negative tuberculin may be a reflection of the total paucity of immunologic response of the patient with sarcoidosis rather than a specific aberration of the tuberculin reaction.[5] Furthermore, as indicated previously, no consistently reproducible isolations of tubercle bacilli or successful animal transmission studies have been recorded. Another bit of evidence against the common relationship between the two diseases is the beneficial effects of cortisone and ACTH on sarcoidosis and the deleterious effects of these agents on many patients with tuberculosis. We have administered cortisone for as long as four months to 12 patients with sarcoidosis; and, in follow-up studies extending to two and one-half years after medication was discontinued, have failed to observe the development of tuberculosis in a single instance.[6] Further evidences against the tuberculous etiology of sarcoidosis will be presented in the section on epidemiology.

Other interesting etiologic concepts have been offered. Among them are Refvem's[7] suggestions that the inhalation of particulate mineral particles causes the lesions and Teilum's proposal[8] that sarcoidosis is a disease concerned with the "immune mechanism" because of the finding of so-called paraamyloid in sarcoid lesions comparable with that seen in certain of the collagen diseases.

Our interests in etiology have centered around certain epidemiologic features. We have analyzed 300 cases of sarcoidosis that occurred in members of the armed services during World War II.[11] They met all the clinical criteria set up by the panel on sarcoidosis of the National Research Council. A biopsy from each patient was consistent with the diagnosis. A study of birthplaces and induction residencies of these cases has shown that the majority of them were born or spent the major part of their lives in the Southeastern United States. A breakdown of the figures of incidence by regions makes this more apparent. (Table 1) An additional feature of interest is the significantly higher incidence of sarcoidosis in this series in the Negro as compared with the white. As shown in Table 1, this is consistently between 22 to 1 and 18 to 1 when analyzed according to regions of the United States. This will explain in part, but not entirely, the geographic distribution of these cases. It

| Region | RATES PER 100,000 INDUCTEES | | | Negro/White Ratio |
|---|---|---|---|---|
| | Total | White | Negro | |
| I | 5.8 | 1.2 | 21.5 | 18 |
| II | 1.4 | .58 | 13.0 | 22 |
| III | 1.63 | .37 | 8.4 | 24 |

*Table 1—Rates for sarcoidosis. Divided according to following: I. South Atlantic and Gulf Coast states; II. Middle Atlantic and Border States; III. New England, North Central, West.*

was further noted that the lifelong residence of a majority of these patients was in rural rather than urban areas.

In an attempt to refine and to assess the significances of the geographical distribution, other studies were undertaken in conjunction with Doctor John Gentry and, later, Doctor Harold Nitowsky, both members of the Epidemiologic Section, Communicable Disease Center, United States Public Health Service. In brief, it has been shown that a majority of these cases have had residences below the Fall line. This is the area of the continental United States which was under water in comparatively recent geogologic times. A fine, sandy, surface soil is characteristic of this area. Containing beryllium among other elements, these geological formations warrant further study in relation to sarcoidosis. However, in addition to particular soils, certain plants, fungi, or, indeed, bacteria may be indigenous to these areas. Whether such refinements as soil types will contribute significantly to our knowledge of sarcoidosis remains to be seen. We feel, however, that the epidemiologic features, particularly the geographical and racial patterns, are of considerable significance in our understanding of the etiology of sarcoidosis.

The *diagnosis of sarcoidosis* is relatively simple in many cases, particularly when a high index of suspicion is maintained. However, it is becoming increasingly apparent that many cases so diagnosed have been proved to be otherwise as more knowledge of granulomatous diseases accumulates. It is convenient to keep in mind a rather simplified definition of sarcoidosis when considering such a diagnosis, ". . . a granulomatous disease of *unknown* etiology with a predilection of lesions for the lungs, lymph nodes, eyes, reticulo-endothelial system, skin, and bones." The essential feature is "of unknown etiology" as I shall attempt to show.

The clinical features of sarcoidosis are well-known to all. It may run the gamut from a completely asymptomatic involvement of one or two organ systems to a rapidly fatal disseminated disease. Suffice it to say that any organ or tissue of the body can be invaded by the sarcoid tissue with a variety of seemingly unrelated syndromes ensuing. A comprehensive dissertation on clinical features may be found in the recent scholarly review of Longcope and Freiman.[3] The elevated serum proteins and the peripheral eosinophilia variably noted in active cases are merely ancillary diagnostic aids. Similarly, the roentgenographic appearance of the lungs, while highly suggestive of sarcoidosis, are by no means specific. For example, the miliary infiltrates can be simulated by a variety of entities. Similarly, the appearance of hilar adenopathy, and in particular

the enlarged paratracheal nodes, can be seen in other entities involving the lymphatic structures. The punched-out lesions in the phalanges, while simulated to a certain extent by those of rheumatoid arthritis and gout, are quite helpful when found as they are in approximately 20 per cent of the cases. To date, these bone lesions have not been described in cases of beryllium granulomatosis and histoplasmosis, diseases which in some forms may be confused clinically and pathologically with sarcoidosis.

The biopsy of a lymph node or of other tissue containing the sarcoid tissue is the *sine qua non* of diagnosis. The total picture of the non-caseating granuloma is not specific; neither are the asteroid bodies which may be noted in lesions of leprosy, cryptococcosis, and many foreign body granulomata; nor are the Schaumann bodies also noted in, among others, beryllium granulomata. Taking the total histologic picture into account, it should be apparent that a variety of entities of known etiology may at times provoke a granulomatous tissue reaction not at all dissimilar to that noted in sarcoidosis. Among such diseases are histoplasmosis, beryllium granulomatosis, traumatic lesions, reaction to nematodes, mycotic infections, non-caseating tuberculosis, and the lymph nodes draining a carcinoma, to mention a few. That a node with the "sarcoid" reaction does not come from a patient with sarcoidosis is obvious in many instances. However, recent information has clearly demonstrated that some patients with clinical pictures consistent with and histologic features compatible with sarcoidosis have granulomatous disease of known etiology; e.g., histoplasmosis and the delayed chemical pneumonitis of beryllium workers.[9, 10]

Another diagnostic test of considerable interest is the Kveim reaction. This depends upon the development at the site of the intracutaneous inoculation of a suspension of "sarcoid tissue" of a slowly growing lesion which on biopsy has the histologic features of "sarcoid." In our experience, we have noted no false positive reactions and have obtained a positive reaction in all cases of active sarcoidosis on whom the test has been performed. The principal drawback of the Kveim reaction is the time element. Four to six weeks is usually required for the reaction to become apparent. However, in some reported instances, as long as 18 months have been reported—quite a long time to wait for a skin reaction. To my knowledge, a positive reaction has not been obtained in any patient with beryllium disease or with histoplasmosis.

## CONCLUSIONS

Recognizing the confusion and many pitfalls, how, then, does one make the diagnosis? How is one certain that a patient has sarcoidosis and not merely a "sarcoid." In essence, only by taking into account the total picture (clinical features, x-ray findings, results of biopsy, course of the disease, contacts with beryllium, and the like), and in particular by keeping in mind that at the present time the etiology is unknown can this be accomplished. Diseases of now known etiologies, but with features similar to those of sarcoidosis, should not be so categorized; e.g., beryllium disease and histoplasmosis.

## RESUMEN

Reconociéndose la confusión y las muchas posibilidades de error, como entonces hacer diagnóstico? Como puede uno estar cierto de que un enfermo tiene sarcoidosis y no solo un "sarcoide."

Esencialmente, solo tomando en consideración el cuadro completo (caracteristicas clínicas, hallazgos a los rayos X, resultado de biopsia, evolución de la enfermedad, contacto con beril o y algo semejante) y en particular conservando en la mente que al presente la etiología es desconocida, puede así llegarse al diagnóstico?

No deben confundirse con las enfermedades que ahora son de etiología conocida y que tienen características semejantes tales como la enfermedad provocada por el berilio y la histoplasmosis.

## RESUME

Etant donné la complexité et les nombreuses causes d'erreurs, comment peut-on faire le diagnostic, comment peut-on être certain qu'un malade est atteint de sarcoïdose et non simplement de "sarcoide"? Peut-on y arriver simplement en prenant en considération le tableau clinique dans son ensemble (constatations cliniques, aspect radiologique, résultats de la biopsie, évolution de l'affection exposition au béryllium ou autres substances de cet ordre) et en particulier en gardant à l'esprit que pour le moment l'étiologie est inconnue? Des affections dont l'étiologie est actuellement connue mais dont les symptômes se rapprochent de la sarcoidose ne devraient pas être catégorisées comme telles. Il en est ainsi de l'histoplastome et de la bérylliose.


## REFERENCES


1 Jaques, W. E.: "Sarcoidosis. A review and a proposed etiologic concept," *Arch. Path.*, 53:558, 1952.

2 Riley, E. A.: "Boeck's sarcoid. A review based upon a clinical study of fifty-two cases, *Am. Rev. Tub.*, 62:231, 1950.

3 Longcope, W. T. and Freiman, D. G.: "A study of sarcoidosis," *Med.*, 31:1, 1952.

4 Lemming, R.: "An attempt to analyze the tuberculin anergy in Schaumann's Disease (Boeck's "Sarcoid") and uveoparotid fever by means of BCG vaccination," *Scan.*, 103:400, 1940.

5 Friou, G. J.: "A study of the cutaneous reactions to oidiomycin, trichophytia, and mumps skin test antigens in patients with sarcoidosis," *Yale Jour. Biol. & Med.*, 24:533, 1952.

6 Michael, M. Jr.: "The treatment of sarcoidosis with cortisone. (Symposium on Cortisone and ACTH)," *Tr. of the 47th Annual Meeting of the Nat. Tub. Assn.*, 1951.

7 Refvem, O.: "Chronic granulomas in alimentary tract caused by minute mineral particles: "Boeck's disease" and occurrence of minute mineral particles (preliminary report)," *Acta. path. et microbiol., Scan.*, 25:107, 1948.

8 Teilum, G.: "Allergic hyperglobulinosis and hyalinosis (paramyloidosis) in the reticulo-endothelial system in Boeck's sarcoid and other conditions. A morphologic immunity reaction," *Am. Jour. Path.*, 24:389, 1948.

9 Pinkerton, H. and Iverson, L.: "Histoplasmosis—Three fatal cases with disseminated sarcoid-like lesions," *Arch. Int. Med.*, 90:456, 1952.

10 Hardy, H. L. and Tabershaw, I. R.: "Delayed chemical pneumonitis occurring in workers exposed to beryllium compounds," *Jour. Indust. Hyg. and Toxicol.*, 30: 228, 1948.

11 Michael, M. Jr., Cole, R. M., Beeson, P. B. and Olson, B. J.: "Sarcoidosis: Preliminary report of 350 cases with special reference to epidemiology," *Am. Rev. Tub.*, 62:403, 1950.

# The Value of the Routine Chest X-ray Film in Detecting Diaphragmatic Hernia; A Report of 53 Cases.[1]

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The increasing use of the x-ray film inspection of the chest in mass surveys on a national scale and in routine examinations of hospital admissions has uncovered an enormous amount of pathological material. The x-ray film of the chest has proved indispensable in detecting pulmonary tuberculosis and carcinoma. The purpose of this paper is: (1) to point out that the routine chest film is useful in detecting diaphragmatic hernia and (2) to outline the criteria that would lead one to suspect this condition.

During the years 1950-1952 inclusive, 80,000 routine chest films were taken of the resident patients, new admissions and employees of the Manteno State Hospital. This group represented a total of 17,076 persons. In reading these x-rays, 53 cases of diaphragmatic hernia were discovered; 98% of these were of the esophageal hiatus type. These 53 cases gave an incidence of 0.31 per cent or a rate of 31 per 10,000 persons surveyed. None were sent to the x-ray department because of symptoms or physical findings suggestive of diaphragmatic hernia.

The age incidence was as follows:

| | |
|---|---|
| 30- 40 years | 3 |
| 40- 50 years | 1 |
| 50- 60 years | 5 |
| 60- 70 years | 17 |
| 70- 80 years | 17 |
| 80- 90 years | 9 |
| 90-100 years | 1 |

Thus a majority of the cases occurred between the ages of 60 and 80 years.

The first roentgenological study of diaphragmatic hernia in which the importance of the routine chest film was stressed was that of Carman and Fineman in 1924. Nemec stressed the importance of variations in density within the cardiac shadow and stated that it was usually due to herniation of the stomach through the diaphragm.

The following criteria have proved successful in the detection of diaphragmatic hernia in the routine chest x-ray film. First, the absence of a stomach bubble or magenblase below the left diaphragm. This is a finding common to nearly all cases. In those hernias however, that are readily

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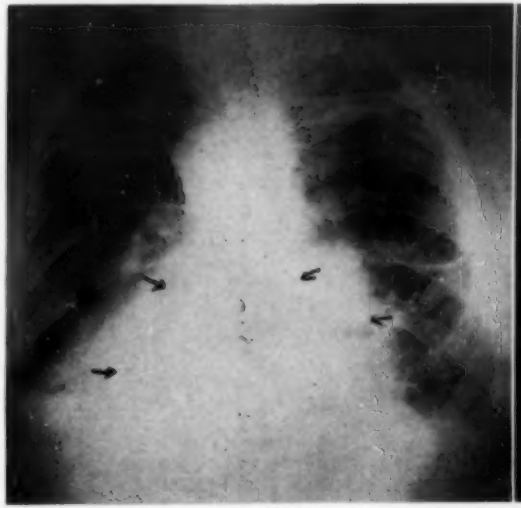

FIGURE 1

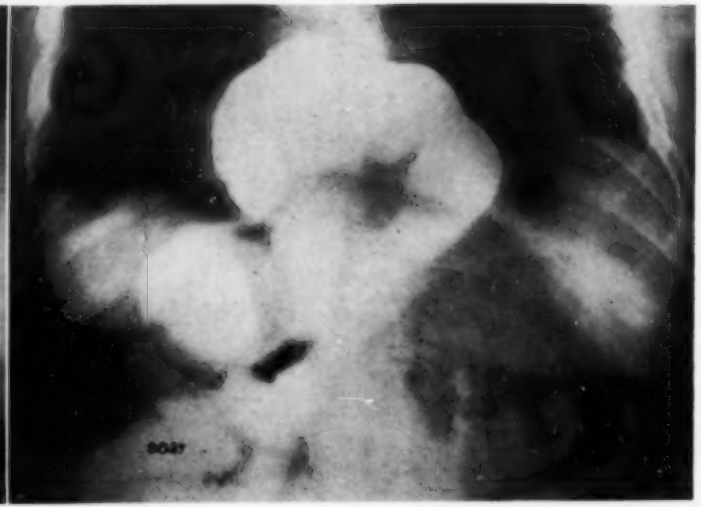

FIGURE 1A

*Figure 1*: An enlarged heart silhouette containing a large air pocket with fluid level which occupies both the right and left heart shadows. *Figure 1A*: Barium meal studies revealed a large hiatal hernia consisting of almost the entire stomach.

reducible, the magenblase will be apparent at times in the films taken in the upright position. Second, the enlarged square-shaped or globular heart silhouette. This most commonly involves the left ventricular shadow but the enlargement may also extend to the right. This deformed heart shadow may contain a large air pocket with horizontal fluid level in one case, Fig. 1; a prominent air pocket without fluid level in another case, Fig. 2; a faint air bubble in a third case, Fig. 3; or just streaks of air along the border of the left or right ventricle in a fourth case. The third possibility is the ovoid, elongated homogeneous density lying within the lowermost portion of the center of the heart silhouette. This shadow appears to be a part of the lower portion of a dilated thoracic aorta but it continues to merge broadly with the subdiaphragmatic shadow instead

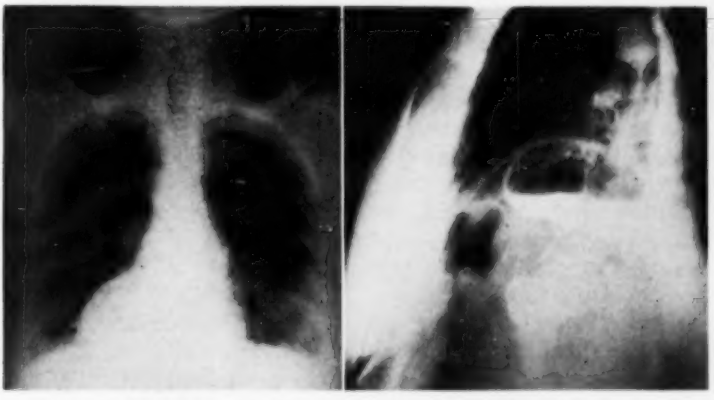

FIGURE 2 FIGURE 2A

*Figure 2*: Demonstrates an enlarged square-shaped heart containing a prominent air pocket without a fluid level. *Figure 2A*: Demonstrates the barium filled stomach, inverted within the chest.

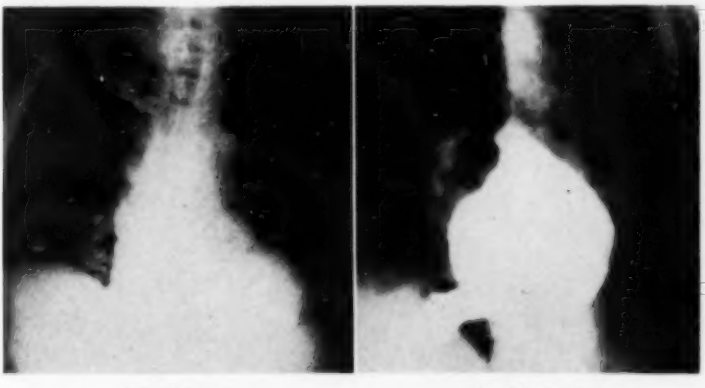

FIGURE 3 FIGURE 3A

*Figure 3*: Demonstrates a small horizontal air bubble lying on the left heart border. The heart is enlarged and square-shaped. *Figure 3A*: Barium studies of Figure 3.

of becoming narrower as it enters the aortic opening of the diaphragm. This shadow does not alter the shape of the heart and does not contain air bubbles or fluid levels, Fig. 4. Fourth, the massive density occupying the lower lung field, obscuring the diaphragm and also continuous with the subdiaphragmatic shadow. This massive density may contain irregular air pockets or may be homogeneous, Fig. 5.

Alterations in the contour of the diaphragm such as tenting, peaking, and waves of various sizes which frequently lead one to suspect possible herniation, will produce only negligible yields of positive diagnosis on the completion of the barium studies. There are instances wherein diaphragmatic hernia and partial elevations of the diaphragm and even marked eventrations may coexist. The hiatal hernias per se do not occupy these deformities of the diaphragm.

The differences in diaphragmatic excursions on fluoroscopy which are described by so many writers as indicative of herniation are present only in few of the cases. According to Jenkinson, if these differences in diaphragmatic motion are depended upon to make a diagnosis, most of the cases will be missed. It is also possible that a hernia may shift its position so that at one time an examination will show the stomach below the diaphragm while at another time, the presence of the hernia will be obvious in the chest. In several instances in this series, the barium-filled stomach, during fluoroscopy, herniated momentarily and reduced itself spontaneously even in the prone position. Repeated examinations are therefore advisable in some cases.

I am deeply indebted to Dr. Roy Kegerreis, consultant radiologist at Manteno State Hospital for conducting the barium studies in this group of cases. The technique employed consisted of ingestion of a barium meal followed shortly thereafter by films taken in the Trendelenburg position, either prone or supine. Films were also taken in the oblique and lateral

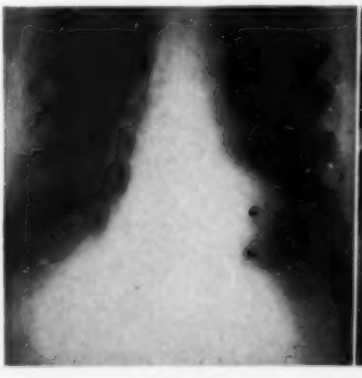

FIGURE 4

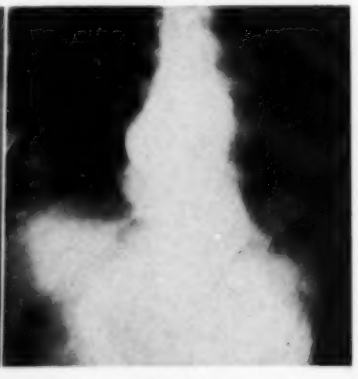

FIGURE 4A

*Figure 4*: Demonstrates an ovoid homogeneous shadow which appears to be a part of the lower portion of the thoracic aorta. It does not contain air bubbles or a fluid level. Also shows coexistence of a peaked right diaphragm. *Figure 4A*: Demonstrates a large part of the stomach within the cardiac shadow.

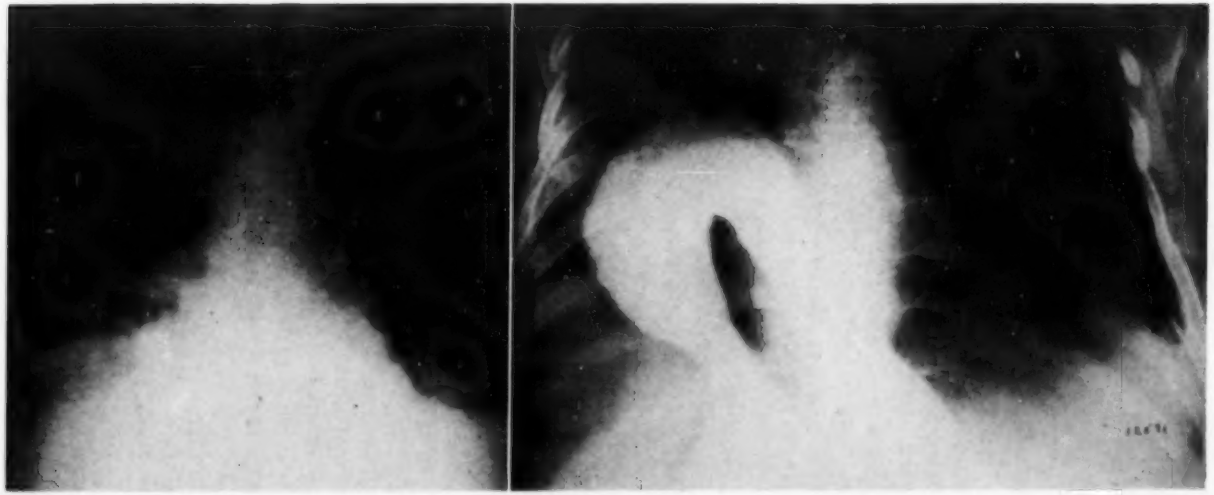

FIGURE 5 FIGURE 5A

*Figure 5*: Demonstrates a large ovoid density occupying the left lower lung field and also continuous with the subdiaphragmatic shadow. The heart is displaced to the right. *Figure 5A*: Barium enema: A large loop of bowel forms the shadow in the lower chest and is located anteriorly. This is a hernia of the Morgagni type.

positions. Abdominal pressure was applied in nearly all of the cases and the patient was instructed to cough. In several instances wherein the barium meal failed to confirm the suspicion of herniated loops of bowel in the chest, a barium enema was done and the diagnosis was confirmed. The employment of pneumoperitoneum as a diagnostic aid in those cases wherein herniation of omentum or part of the liver is suspected will prove informative.

## CONCLUSIONS

1. The routine chest x-ray is useful in the diagnosis of diaphragmatic hernia.
2. The finding of an enlarged square-shaped or globular heart silhouette containing a large air pocket with or without a horizontal fluid level, is virtually diagnostic of hiatal hernia.
3. Small faint air bubbles or streaks of air along the right or left borders of the heart should also be suspected of hiatal hernia.
4. The ovoid elongated homogeneous shadow that produces variations in density within the cardiac silhouette is usually due to a hiatal hernia.
5. Any massive shadow within the lung field, continuous with the diaphragmatic outline and obscuring it, or any shadow in which the continuity is incomplete above the diaphragm, is suspicious of diaphragmatic hernia of the Morgagni type or one of traumatic origin.
6. The use of the barium meal and/or barium enema is obligatory for the final confirmation of the suspected condition.
7. Diagnostic pneumoperitoneum may be employed in those cases wherein herniation of omentum or part of the liver is suspected.

## RESUMEN

1.—La radiografía ordinaria de tórax, es útil para diagnosticar la hernia diafragmática.

2.—El hallazgo de una imagen cardiaca crecida o de forma cuadrangular o globular conteniendo una gran bolsa de aire con o sin nivel líquido, es virtualmente de valor diagnóstico en la hernia hiatal.

3.—Pequeñas burbujas de aire o fajas de aire a lo largo del borde derecho o izquierdo del corazón, deben también hacer sospechar la hernia del hiatus.

4.—La forma ovoide alargada de la imagen cardiaca, homogénea, que produce variaciones de densidad dentro de la misma imagen cardiaca, es habitualmente debida a hernia del hiatus.

5.—Cualquier sombra masiva dentro del campo pulmonar, en continuidad con el diafragma y que obscurece a éste, o cualquier sombra en la que la continuidad es incompleta arriba del diafragma, es sospechosa de—hernia del diafragma del tipo Morgagni o de origen traumático.

6.—El uso de la comida de bario y/o del enema de bario, es obligatorio para la confirmación final de esta condición patológica.

7.—El neumoperitoneo diagnóstico, puede emplearse en aquellos-casos en los que se sospecha una hernia del omento o de parte del hígado.

## RESUME

1.—Les examens radiologiques de routine permettent le diagnostic de hernie diaphragmatique.

2.—La constatation d'une silhouette cardiaque hypertrophiée, d'apparence quadrangulaire ou globuleuse, contenant une vaste poche d'air avec ou sans niveau liquide horizontal, affirme pratiquement le diagnostic de hernie diaphragmatique.

3.—Des bulles d'air discrètes ou des bandes gazeuses le long des bords droit et gauche du coeur doivent aussi le faire suspecter.

4.—L'ombre ovalaire, allongée et homogène, provoquant des variations dans la densité de la silhouette cardiaque est habituellement due à une hernie diaphragmatique.

5.—Toute ombre massive du champ pulmonaire attenante à l'ombre diaphragmatique et l'obscurcissant, toute ombre qui ne se continue pas dans sa totalité au-dessous du diaphragme peut faire soupçonner une hernie diaphragmatique du type de Morgagni ou une hernie d'origine traumatique.

6.—Il faut obligatoirement avoir recours à la bouillie ou aux lavements barytés pour confirmer le diagnostic.

7.—Le pneumopéritoine peut être utilisé dans un but de diagnostic quand on suspecte une hernie de l'épiploon ou d'une partie du foie.

NOTE: The author wishes to express his thanks to Dr. E. L. Jenkinson, Director of Radiology, St. Lukes Hospital, Chicago, for his many helpful suggestions and to Dr. Alfred P. Bay, Manager of Manteno State Hospital for the statistical studies.

## REFERENCES

1 Carman, R. D. and Fineman, S.: "The Roentgenologic Diagnosis of Diaphragmatic Hernia with a Report of Seventeen Cases," *Radiology*, 3:26, 1924.

2 Nemec, Stanley S.: "Differential Diagnosis of Retrocardiac Shadows," *Radiology*, 50:174, 1948.

3 Harrington, Stuart W.: "Roentgenologic Considerations in the Diagnosis and Treatment of Diaphragmatic Hernia," *Am. Jour. of Roent.* 49:185, 1943.

4 Jenkinson, E. L.: "Lesions of the Diaphragm," *Am. Jour. of Roent.*, 14:16, 1925.

# Plastic Bronchitis

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For many centuries physicians have been interested in the body secretions both in health and disease. This has been especially the case in those secretions that are readily available such as sputum.

The earliest mention of plastic bronchitis is by Galen (A. D. 131-200). The great John Hunter (1728-1793) mentions one case in a young man. In this particular instance the patient began to cough up casts following on a "severe course of mercury." Hunter was interested enough in the case to have an excellent engraving made of a bronchial cast coughed up by this patient. One of the great difficulties in identifying these cases in the literature before the advent of the 19th Century, is that these structures are often referred to as "bronchial polyps." There were even more fanciful ideas, Tulpius and Bartholine (quoted North) were of the opinion that these structures consisted of the "blood vessels of the lung." Morgagni (quoted North) was much nearer the truth when he postulated that these structures consisted of "Inspissated bronchial mucus, the thinner parts of the mucus being carried off by the constant current of air."

The total number of cases of plastic bronchitis that I have been able to trace in the literature is 232. The vast majority of them have been recorded in the 19th Century. One of the best documented articles about this peculiar condition is that by Bettman (1902).

Most of the authors divide their cases into symptomatic and idiopathic, with a further division into acute and chronic. From a perusal of these cases it is obvious that this classification is only thus fashioned for a matter of convenience, as many of these cases were originally described at a time when accurate differential diagnosis was difficult. It may well be that there was an unrecognized secondary factor present in many of these so called idiopathic cases. Again some of the chronic cases present with acute episodes.

In many of the 232 cases the condition alone was mentioned without any details being given, but I have been able to obtain reasonable records of 59 of them including four collected by myself. From a study of these cases the following features emerge. This condition is found at all ages; the youngest patient was aged 10 months and the oldest 75 years. Many authors hold that the condition is more common in women than in men.

TABLE 1

| Age Years | Female | Male | Total |
|---|---|---|---|
| 0- 9 | 0 | 2 | 2 |
| 10-19 | 6 | 3 | 9 |
| 20-29 | 8 | 5 | 13 |
| 30-39 | 3 | 1 | 4 |
| 40-49 | 8 | 5 | 13 |
| 50-59 | 3 | 7 | 10 |
| 60+ | 2 | 1 | 3 |

In this particular series, in those cases where the sex was noted there were 30 women and 24 men (Table 1).

With few exceptions, where there was an associated condition the respiratory tract was directly affected, and was one of the main sites of the complicating disease. The most commonly occurring complicating diseases were pulmonary tuberculosis, heart disease and asthma, in that order. The majority of the cardiac cases had a rheumatic etiology.

As noted previously, the condition may arise as a complication of an already existing condition or it may arise de novo. The onset may be dramatic or insidious. In most of the cases some of the following features occur: fever, malaise, constant irritating cough, pain in the chest which may be of a pleuritic nature or be described as a deep ache. There is often much respiratory distress in the more acute phases, a respiratory wheeze may be present and it is peculiar in that it is an inspiratory stridor so different from the expiratory stridor so commonly found in cases of asthma.

The sputum may be nearly clear or frankly purulent and it contains the characteristic casts of the bronchial tree as found in this condition, sometimes it is blood stained.

Bleeding may be considerable or it may be confined to a moderate degree of blood staining to the exterior of the casts. The casts themselves vary from fawn to white in color, and often in the fresh state have a cuff of clear mucus and exhibit the typical branching. There is usually a diffuse bronchitis throughout the lungs, which may be associated with the signs of partial or complete pulmonary atelectasis and at times with evidence of overlying pleurisy. "Bruit de drapeau" though cited by various authors as a sign in this condition was not heard.

Radiologically there are often no abnormal features, though there may be evidence of atelectasis. On other occasions persistent failure to dislodge a cast may lead to the formation of lung abscess. Some of the cases of this condition are associated with bronchiectasis. It is difficult to be sure which came first, the bronchiectasis or the plastic bronchitis, but in a proportion of the cases I believe that the former may well be the result of the latter.

There have been few cases in which bronchoscopy has been carried out. In one case there was noted excessive mucus and the bronchi appeared to be in spasm (Beaumont 1950), and in another the bronchi contained mucopurulent sputum but appeared otherwise normal (Merica 1950). In one of my own cases there was a considerable amount of thick mucus in the bronchi but no other abnormality.

Treatment in this condition has run through the whole spectrum of therapeutic possibilities thereby indicating that up to the present there is no easy road to success. Fortunately in quite a number of the cases the condition resolves spontaneously. In those cases in which there are recurrent attacks the condition can only be treated symptomatically during the more acute phases by keeping the sputum as liquid as possible by steam inhalations and mixtures containing potassium iodide; and, in addition, by treating any secondary infection with the appropriate chemo-

therapeutic agent. On very rare occasions some authors have found it necessary to employ a bronchoscope to remove a persistently impacted cast.

Death is often caused by the associated condition; that is to say heart failure, pulmonary tuberculosis, asthma or some other such state. Deaths due to plastic bronchitis *per se* are decidely unusual. I could only find two references to death as a result of a cast blocking major bronchi (Andral 1889, Johnstone 1945). It is possible that the casts stick so rarely on account of the very thick slippery mucus cuff possessed by the majority.

The course of the illness is variable; the patient may have a single

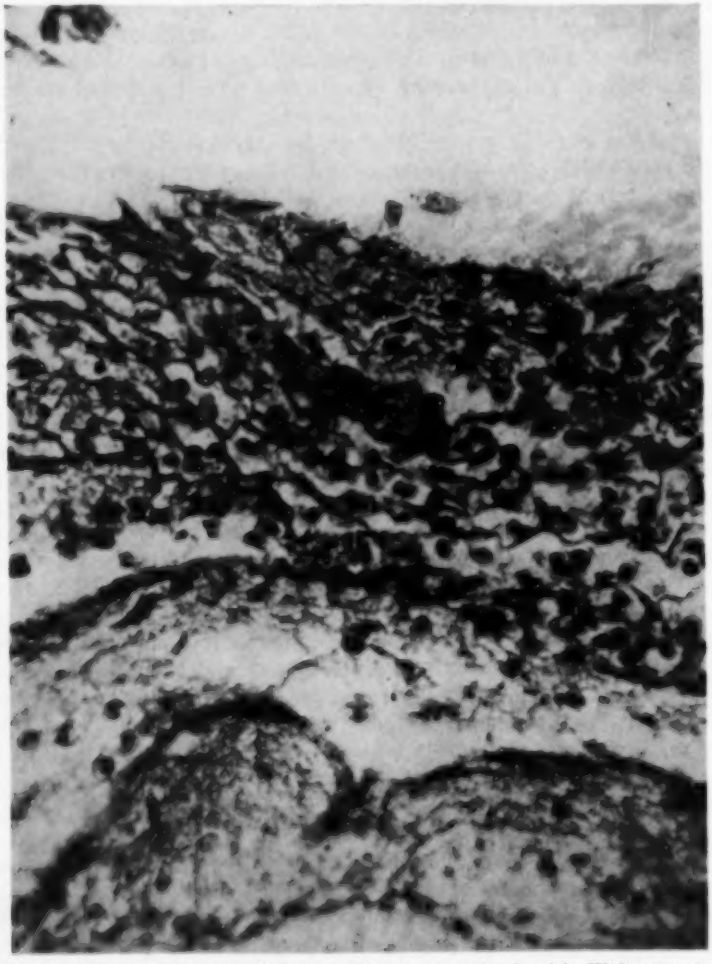

FIGURE 1: Photomicrograph of a bronchial cast stained with Weigerts stain. It demonstrates the fibrillary nature of the casts and the cellular exudate between the fibrils. × 90.

attack and never be troubled again, the attacks may recur over a period of weeks and then cease, or they may appear again and again for many years. (North 1838, Bettman 1902, Schwarzkopf 1904, Shoyer 1906, West 1908, Josué 1909, Laurie 1915, Beaumont 1950, Crofton 1952). In one of my own cases the patient had been afflicted with the condition for a matter of eight years.

In regard to the structure of the casts there has been considerable difference of opinion. The majority of the authors are in agreement on the laminated fibrillary nature of the casts. Some hold that they consist entirely of fibrin (Dalaché 1903, Rabe 1903, Moser 1904, Ritchie 1904, Shoyer 1906, Hadley 1917, Pappenheimer 1922, Rodenbaugh 1923, Ash 1924, Mulligan 1924, Tuteur 1927, Perlstein 1930, Meyer 1937, Sieler 1942, Johnstone 1945, Rubin 1947, Beaumont 1950, Govoni 1950). Other authors believe that both fibrin and mucin were present (Bettman 1902, Schwarzkopf 1904, Holmes 1908, Lasnier 1909, Christian 1919, Walker 1920, Engel 1926, Stapf 1927, Hart 1928, Izzo 1933, Rakower 1938, Boyd 1943, Brewer 1951). A minority of the authors hold the view that the casts might consist of mucin only (Andral 1889 quoted Berkhart, Josué 1909, Lamaison 1922, Fiori 1928). In some cases eosinophils were noted as being present (Holmes 1908, Christian 1919, Merica 1950), and a few red blood cells were also found.

In the four cases personally studied I have confirmed the physical characteristics of the casts. The casts consisted of masses of intertwining fibrils which were of a homogenous consistency (Fig. 1). Among these fibrils were a considerable number of cells. In two this cellular exudate consisted of mononuclear cells. Of the remaining two, in one the cells were neutrophil polymorphonuclear leucocytes, and in the other eosinophil polymorphonuclear leucocytes.

The stains and the methods used were Weigerts stain for fibrin, and Schiffs periodic method for fibrin. The stains used for the identification of mucin were thionin and mucicarmine. They proved to be unsatisfactory with the material used so that the results were inconclusive. In view of this difficulty it was decided to try and obtain the answer by other methods.

To the fragments of bronchial cast from each was added a mixture of fresh plasma and an active fibrinolysin (streptokinase.) The four tubes containing the mixture were then incubated for some hours at 37° C. In none of the tubes was there evidence of digestion of the casts. It had previously been proved that the enzyme could quite easily digest pure fibrin.

The casts were soluble in 3 per cent NaOH and in a saturated solution of Na2CO3. The casts were boiled for 1-1½ hours with 20 per cent v/v HCl. After neutralisation of the hydrolysate with solid sodium carbonate, equal portions were boiled with Benedicts solution.

In one of the cases (A. G.) more extensive investigations were carried out. The biuret reaction was positive indicating the presence of polypeptides. A Kjeldahl estimation gave a result of 3.7 per cent nitrogen. Following on the hydrolysis of the cast by hydrochloric acid, the hydrolysate was neutralised and by the use of phenylhydrazine two osazones were formed. One was glucosazone and the other probably the osazone of man-

nose. Addition of a solution of barium chloride to the hydrolysate produced a slight precipitate indicating the presence of a sulphate radicle. It is of interest to note that gastric mucin contains 4 per cent nitrogen (Meyer 1938), while pure fibrin contains 16 per cent. Gastric mucin also contains glucose and a sulphate radicle. It would appear that these casts are in the nature of an acid mucopolysaccharide, probably similar to mucin (Table 2).

TABLE 2

| | Fibrin | Gastric Mucin | Casts |
|---|---|---|---|
| Nitrogen | 16 per cent | 3-4 per cent | 3.8 per cent |
| Glucose | — | + | + |
| Sulphur | — | + | + |
| Streptokinase | Digested | No Action | No Action |

In the few cases in the literature that came to autopsy none of the authors mention anything special about the pathology of the lungs. In one of my patients (A. G.) the left lower lobe and lingula were removed on account of bronchiectasis. Examination of the removed portions of lung revealed the typical appearances of infected bronchiectasis with normal apical lower subsegment. In particular where the bronchi were not bronchiectatic there was no evidence of any other abnormality.

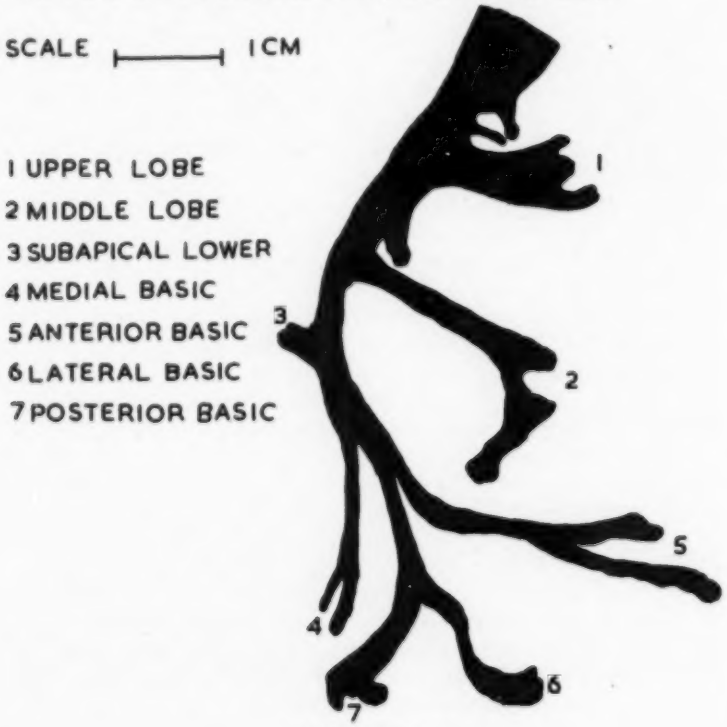


FIGURE 2

*Case 1:* A. G. female, aged 11 years, had been troubled by productive cough since the age of three years. The sputum was purulent and contained bronchial casts. These symptoms persisted unchanged throughout the year. She used to cough up four or five casts of varying sizes during the day. She noted, as did her mother, that the casts on occasion were blood stained. She never had real difficulty in coughing up these casts or forewarning that one was going to appear. Antihistamines and mixtures containing potassium iodide were tried without improvement in her condition. Investigations revealed that in addition she was suffering from bilateral bronchiectasis affecting the right lower and middle lobes and left lower lobe and lingula. As bronchiectasis was considerably worse on the left side than the right it was decided to carry out a resection of the affected portions of lung on the left side. This was done and although the amount of sputum was decreased and the purulent element removed, the plastic bronchitis was unchanged. Shortly after the lobectomy, during the immediate postoperative period, she developed pneumonitis on the right side accompanied by a moderate amount of atelectasis. This whole condition cleared up following the coughing up of a large bronchial cast, consisting of the greater part of the bronchial tree.

*Case 2:* A male aged 56 years following a haemoptysis in 1937 was found to have bilateral apical pulmonary tuberculosis. There was recurrence of symptoms in 1941 and he was treated with a short period bed rest but no other active therapeutic measures were undertaken.

Shortly after this he began to have attacks of bronchitis accompanied by coughing up bronchial casts. When they appeared these attacks lasted from four to six weeks.

In January 1951 he had an acute pulmonary episode associated with rigors. This was terminated by the coughing up of a bronchial cast which was quickly followed by a considerable amount of purulent sputum with the disappearance of acute pulmonary symptoms.

His attack in December 1951 began as usual with a dry cough accompanied by fever and retrosternal discomfort. Within a short time the cough became productive with purulent sputum containing casts. Clinically he was wheezy, slightly cyanosed, there were moist sounds over both upper lobes and rhonchi over the right upper lobe.

Radiologically there was a fresh inflammatory lesion in the right upper lobe. His fever was controlled by the use of penicillin but he continued to have bronchitis symptoms and to cough up casts for a further 12 weeks. These casts were several centimeters in length, fawn in color and showed branching.

An x-ray film taken on March 28, 1952 revealed practically complete clearing of the fresh lesion in the right upper lobe.

*Case 3:* E. P., a female, aged 43 years developed asthma following a period of very severe domestic worry and stress three years prior to admission in April 1950. During an asthmatic attack her sputum contained branching casts both solid and tubular, two to three centimeters long. Even between asthmatic attacks she occasionally coughed up bronchial casts. The coughing up of a cast was sometimes preceded by a dragging pain in the right upper chest. After a year her domestic worries decreased and the asthmatic attacks became less frequent.

Nine months prior to admission she became ill with fever, rigors, sweating, and a productive cough accompanied by fetid sputum. Radiologically there were inflammatory changes in the mid zones of both lungs. She was treated with large doses of penicillin and as a result her symptoms resolved.

Eight months later she developed cough accompanied by dragging pain in the right upper chest anteriorly. After a period of strenuous coughing she managed to cough up a thick white cast. Immediately following this there appeared gelatinous blood stained sputum. Radiologically there was partial atelectasis of the anterior segment of the right upper lobe. Over the next two months this atelectatic segment gradually underwent reaeration. Clinically the signs were those of mild bronchitis. The blood picture was normal throughout. Bronchography revealed bilateral bronchiectasis of moderate extent, in the anterior and lingula segments of the left upper lobe and in an area on the right side which may be the middle lobe. Although the bronchograms were not satisfactory they were not repeated as she was not a good subject for this form of investigation. Bronchoscopically the bronchi contained considerable amounts of thick mucus but there was no evidence of other abnormality. Although her asthmatic symptoms responded to symptomatic therapy she still continued to cough up casts intermittently.

Since her discharge from hospital her asthmatic symptoms have shown a further gradual improvement concomitantly with an improvement in her domestic environment.

*Case 4:* E. S., a male, aged 41 years was a perfectly healthy individual until six weeks before he was seen, when he developed fever accompanied by cough. In the first instance he was treated with one of the sulfonamides but this was stopped on account of vomiting. In its place he was given penicillin 800,000 units per day and in addition chloromycetin 3 gm. per day. His fever settled but he became much more wheezy and his sputum was thick and streaked with purulent material. Within a week of the

new therapy he began to cough up large numbers of branching casts, varying in length from 1 to 6 cm. In view of these symptoms therapy was stopped though he continued to bring up casts. He had considerable inspiratory stridor and sleep was made difficult on account of breathlessness. These casts were not easy to bring up and he had prolonged bouts of useless coughing. In spite of severe respiratory symptoms his chest was radiologically normal. Clinically there was no evidence of over-expansion of the chest but there were scattered rhonchi over all areas. In view of the fact that he had been given a considerable amount of mixed antibiotics in association with sulfonamides, his sputum was cultured for fungi with negative results.

Over the next six weeks there was a gradual improvement in symptoms so that at the end of this period he was able to be up and about although he still had evidence of some bronchitis and was coughing up an occasional cast. The casts finally ceased to appear; and he has remained in good health.

### *Discussion*

It is well known that the organism Corynebacterium diphtheria can affect the greater part of the respiratory tract and can on occasion be responsible for the formation of bronchial casts, but in this discussion casts formed in this manner are excluded.

There have been many theories as to the etiology of bronchial casts in plastic bronchitis. Some authors are of the opinion that infection is the important underlying feature (Ritchie 1904, Schwarz 1908, Mulligan 1924). Against this theory is the fact that there has never been a predominant organism constantly present. Other authorities believe that hemorrhage plays a major part in this formation (Dalaché 1903, Berger 1927). While it is freely admitted that a varying amount of haemorrhage does occur in them the majority show no evidence of haemorrhage. Hypersecretion of the mucin-secreting bronchial glands has been put forward as an important factor (Lamaison 1922, Govoni 1950). This would not explain the apparent increase in the coagulability of the bronchial mucin. One theory advanced to explain this peculiarity, is that persons with plastic bronchitis secrete an abnormal enzyme "mucinase" which causes mucin to coagulate (Josué 1909). I repeated this author's experiments on several occasions but was unable to demonstrate evidence of such an abnormal enzyme.

For a considerable number of years bronchial casts have been observed in some cases of asthma dying during an attack (Berkhart 1889, Huber 1922, Steinberg 1928). Also Shaw (1951), did thoracotomies on nine cases of asthma for the removal of persistently atelectatic areas of lung, found that the blocking agent in all cases was "a thick plug of white mucus." Certainly there was no difference in the structure of the casts coughed up by my asthmatic patient compared to those coughed up by my other three patients. Asthmatic patients' sputum contains eosinophil leucocytes during an attack, and they have also been found in the sputum of cases with plastic bronchitis (Holmes 1908, Christian 1919, Merica 1950). There were also large numbers of them in the sputum and among the fibrils of the bronchial casts of "E.S." one of my patients. It would therefore appear that plastic bronchitis and asthma have some points in common and that they both might yield to similar therapeutic agents. It was disappointing to find that antihistamine drugs such as phenergan, which has some effect in certain cases of asthma, had no value in plastic bronchitis. In the case of "E.P.", though we could influence her asthma for the better by symp-

tomatic treatment this had no marked effect on the plastic bronchitis. Certain French authors, Lamaison (1922) in particular, record the occurrence of mucous colitis in association with plastic bronchitis. This would suggest that the mucin secreting mechanism is disordered over a much wider area than the respiratory tract.

It would appear that when one considers the constancy of the composition of the casts and the wide variety of diseases found in association with this condition, the only reasonable assumption is that we are dealing with the final common pathway for a large variety of different stimuli. This is a similar concept to grand mal epilepsy, where the number of idiopathic cases is becoming progressively less with increasing refinements of diagnostic procedures.

An individual may be fortunate and only have one attack in his life, though it may last in the first instance for anything up to six weeks, or he may have recurrent attacks over a prolonged period extending into years. The prognosis is frequently that of the underlying condition. But there is a real risk of secondary bronchiectasis occurring, due to persistent atelectasis with distal infection. One of the cases cited "E. P." showed scattered bronchiectasis throughout both of her lungs. There was no evidence of peripheral eosinophilia at any time so it is unlikely that her bronchiectatic condition was secondary to eosinophilic infiltration of the lung. Crofton (1952) found bronchiectatic changes in a female patient who suffered from asthma, eosinophilic infiltration of lung and plastic bronchitis. He was of the opinion that the bronchiectatic changes were secondary to the eosinophilic infiltration. Gough (1952) noted that localized bronchiectasis is a frequent finding in the lungs of asthmatic patients.

Another of my cases "A. G." not only had plastic bronchitis of many years standing but had, in addition, bilateral bronchiectasis.

As the fundamental cause of this condition, the increased coagulability of the bronchial mucin, is unknown, it can only be treated symptomatically. It is most important to be on the alert to prevent casts sticking in the bronchi in order to avoid, as far as possible, the development of bronchiectasis. This is especially important in those chronic cases which carry on over a long period of years. Pain in the chest and fever, with or without radiological evidence of segmental atelectasis, are an indication for vigorous chemotherapy with, in addition, a steam tent, and the use of a mixture containing potassium iodide. The patient should be encouraged to cough. If the atelectatic area does not re-aerate some authors have used a bronchoscope to remove the offending bronchial cast (Merica 1950).

## SUMMARY

Bronchial casts have been found to consist of mucin and the name fibrinous bronchitis should be discarded in favor of plastic bronchitis.

These casts have features in common with those found in subjects suffering from asthma, especially status asthmaticus.

Four case histories are presented.

The condition is the resultant of a variety of different stimuli in a person with particular diathesis.

Prognosis is often that of the underlying condition, though the casts themselves may give rise to recurrent acute inflammatory episodes and, in addition, scattered areas of bronchiectasis.

As the fundamental cause of the increased coagulability of the bronchial mucin is unknown, the condition must be treated symptomatically.

RESUMEN

Se ha encontrado que los moldes bronquiales contienenmucina y que el nombre de bronquitis fibrinosa, debe descartarse en favor de bronquitis plástica.

Estos moldes tienen características comunes con los encontrados en enfermos que sufren de asma, especialmente en estado de mal asmático.

Se presentan cuatro historias clínicas.

Esta afección es el resultado de una variedad de estí—mulos diferentes en una persona con diátesis particular.

El pronóstico es el de la afección de fondo, aunque los moldes por sí, pueden dar nacimiento a episodios recurrentes-inflamatorios, y además, a areas diseminadas de bronquiectasia.

Como la causa fundamental del aumento de la coagulabilidad de la mucina bronquial es desconocida, la afección debe tratarse sintomáticamente.

RESUME

L'auteur a constaté que les moules bronchiques sont constitués par de la mucine et que le terme de bronchite fibrineuse doit être remplacé par celui de bronchite "plastique."

Ces moules bronchiques ont une symptomatologie comparable à celle des moules que l'on peut trouver chez les malades atteints d'asthme et en particulier d'asthme constitutionnel.

L'auteur rapporte quatre observations cliniques.

Cette affection est le résultat d'excitations de différentes sortes sur les individus dont le terrain est particulier. Le pronostic est souvent celui de l'affection sous-jacente, bien que les moules eux-mêmes puissent être à l'origine d'épisodes aigus inflammatoires successifs et de dilatations des bronches disséminées.

Comme la cause véritable de cette coagulabilité anormale de la mucine bronchique n'est pas connue, on ne peut opposer à cette affection qu'un traitement symptomatique.

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BIBLIOGRAPHY

Andral, C. (quoted Berkhart) "Bronchial Asthma" (*London*) *ed.*, 2, 1889.

Ash, B. et al.: "Fibrinous Bronchitis Resembling Tuberculosis of Lung," *Brit. Med. J.*, 1:192, 1924.

Beaumont, G. E.: Applied Medicine," *London*, 141-146, 1950.

Berger, M.: "Beobachtungen uber Unspezifische Haemoptoe im Kindersalter bei der Bronchitis Fibrinosa," *Mschr. Kinderheilk*, 35:145, 1927.

Berkhart, J. B.: "Bronchial Asthma," (*London*) *ed.* 2, 1889.
Bettman, M. :"Report of a Case of Fibrinous Bronchitis with a Review of the Literature," *Am. J. Med. Sciences*, 123:304, 1902.
Boyd, W.: "Textbook of Pathology," 1943.
Brewer, L. A.: "Mucoid Impaction of the Bronchi," *J. Thoracic Surg.*, 22:149, 1951.
Christian, H. K.: "Fibrinous Bronchitis," *Med. Clin. North Amer.*, 2:1255, 1919.
Crofton, J. et al.: "Pulmonary Eosinophilia," *Thorax*, 7:1, 1952.
Dalache, P.: "Contribution to the Study of the Pathogenesis of Bronchial Casts," *Soc. Med. des Hop. de Paris*, 1903.
Engel, H.: "Beitrag zur Bronchitis Fibrinosa Chronica und Ihrem Mikroscopische Sputumbild," *Med. Klinik*, 22:1179, 1926.
Fiori, E.: "Sulla Bronchite Cronica Muco-Plastica," *Riv. Patol. Clin. Tuberc.*, 2:95, 1928.
Galen: (quoted Bettman): "Report of a Case of Fibrinous Bronchitis with a Review of the Literature," *Am. J. Med. Sciences*, 123:304, 1902.
Gough, J.: "Discussion on the Diagnosis of Pulmonary Emphysema," *Proc. Royal Soc. Med.*, 45:576, 1952.
Govoni, A. et al.: "Plastic Bronchitis in Pulmonary Tuberculosis," *Antiseptic Madras*, 47:257, 1950.
Hadley, E. C.: "A Case of Plastic or Fibrinous Bronchitis," *Clin. J.*, 66:267, 1917.
Henke and Lubarsch: "Handbuch der Speziellen Pathologischen Anatomie und Histologie," *Berlin*, 3(1):490, 1928:
Holmes, E. B.: "A Case of Chronic Fibrinous Bronchitis," *New Med. J.* 87:780, 1908.
Huber, J. P. et al.: "Angine a Monocytes et Tracheo-Bronchite Pseudo-Membraneuse," *Ann. Otolaryng. Paris*, 65:784, 1948.
Hunter, J.: "The Collected Works of John Hunter," p. 13, 1837.
Izzo, R. A. et al.: "Bronquitis Fibrinosa," *Rev. Med. Lat.-Amer.*, 19:12, 1933.
Johnstone, D. F.: "Acute Plastic Bronchitis," *Guys Hosp. Gaz.*, 59:2, 1945.
Josue, O. et al.: "Bull. et Mem. de la Soc. Med. des Hopiteaux de Paris," 1909.
Lamaison, C.: "Sur un Cas de Bronchite Muco-Membraneuse," *J. Med. Bordeaux*, 52:569, 1922.
Lasnier, A.: "A Case of Chronic Membraneous Bronchitis," *Bull. Soc. Anat.*, 11:129, 1909.
Laurie, H.: "A Case of Acute Plastic Bronchitis," *Med. J. Aust.*, 1:145, 1915.
Meyer, A.: "Uber Bronchitis Fibrinosa Acuta," *Klin. Wschr.*, 16:1126, 1937.
Meyer, K.: "Cold Spring Harbour Symposia on Quantitative Biology," 6:91, 1938.
Merica, F. W.: "Acute Fibrinous Bronchitis with Massive Atelectasis," *Ohio St. Med. J.*, 46:1079, 1950.
Moser, W. A.: "A Case of Chronic Fibrinous Bronchitis," *New York Med. Rec.*, 66: 216, 1904.
Mulligan, P. B. et al.: "Chronic Fibrinous Bronchitis as a Symptom of Mediastinal Compression," *J. Amer. Med. Ass.*, 82:791, 1924.
North, J.: "Two Cases of Fibrinous Bronchitis," *London Med. Gaz.*, p. 331, 1838.
Pappenheimer: "Ueber einen Fall von Primarer Bronchitis Fibrinosa Chronica," *Med. Klinik*, 18:1557, 1922.
Perlstein, R. N.: "A Case of Fibrinous Bronchitis Complicated by Massive Atelectasis," *Amer. Rev. Tubere.*, 22:82, 1930.
Rakower, J.: "Atelectasie Massive au Cours de la Bronchite Pseudo- Membraneuse Primitive," *Pr. Med.*, 46:1116, 1938.
Ritchie, W.: "A Case of Plastic Bronchitis," *Edinburgh Med. J.*, 15:117, 1904.
Rodenbaugh, F. H.: "Fibrinous Bronchitis," *Amer. J. Roentgenol. n.s.*, 10:843, 1923.
Rubin, E. H.: "Diseases of the Chest," 1947.
Schwarze, R. R.: "Zur Pathologie der Fibrinosin Bronchitis," *Weiner Med. Wschr.*, 58:1178, 1908.
Schwarzkopf, E.: "Ein Fall Bronchitis Fibrinosa Chronica mit Nachweisbarer Lokalisation und Uberweigend aus Schleim bestchenden Bronchialausgussen," *Muench. Med. Wschr.*, 40:343, 1904.
Shoyer, A.: "Phthisis with Fibrinous Bronchitis," *Brit. Med. J.*, 2:1035, 1906.
Seiler, S.: "Ueber Bronchitis Plastica mit Mitteilung eines Durch Kollapstherapie Geheilten Falles," *Schweiz. Med. Wschr.*, 72:86, 1942.
Stapf, A.: "Ueber Bronchitis Fibrinosa und Ihre Bezeihungen zur Lungentuberkulose," *Virchows Arch.*, 263:800, 1927.
Steinberg, B. L. et al.: "Pathology of Bronchial Asthma, Nonbacterial, Allergic and Bacterial Types, Based on Autopsy Material," *J. Lab. and Clin. Med.*, 13:921, 1928.
Tuteur, M.: "Beitrag zur Bronchitis Fibrinosa-Frage," *Beitr. Path. Anat.*, 78:622, 1927.
Walker, C. I.: "Two Cases of Fibrinous Bronchitis with a Review of the Literature," *Amer. J. Med. Sciences*, 159:825, 1920.
West, S.: "Chronic Fibrinous Bronchitis," *Lancet*, 1:489, 1908.

# Clinical Tuberculosis in American Samoa

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Progress in the campaign against tuberculosis among Polynesians living in the South Seas is hampered by a lack of factual information regarding the nature of the disease in the area and of the reaction of the people to it. A great deal of valuable epidemiological work has been done and is in progress under the auspices of the South Pacific Commission and of the several governments concerned, but clinical data are scarce, and usually consist of impressions. For this reason a study was conducted in American Samoa from July 5, 1949 to June 24, 1951 to determine the nature of the tuberculous disease encountered and the response of the Samoans to treatment.

The Samoans inhibit a group of islands which may be found on the map about two-thirds of the way along a line drawn from Honolulu, T. H., to Auckland, New Zealand, somewhat south of the equator. The islands known as American Samoa have a total area of about 76 square miles, and a population now in excess of 18,602, the figure recorded in the U. S. Census, 1950. The climate is warm and moist. Temperature varies but little from 80 degrees (Fahrenheit) throughout the year, and annual average rainfall is 198.4 inches. Despite torrential downpours of rain, however, sunshine is ample. Food is plentiful, although there is possibly a deficiency of protein consumption. Clinical avitaminoses are not seen. Considering the relatively simple demands of existence in the tropics, economic conditions are good. The Samoans are members of the Polynesian race,[1] and in American Samoa are relatively pure representatives thereof, having an admixture of at most 10 per cent Caucasian and 1 per cent Mongoloid blood.

A program designed to control tuberculosis was instituted by the Medical Department of the U. S. Navy in 1921 and has been followed consistently since that time, with some changes in accordance with changing concepts. It has included popular education, case finding surveys employing various forms of tuberculin testing and recently photofluorography, contact examinations, improved hospital and treatment facilities, free treatment, and follow-up clinic. As a result the mortality fell from 347 per 100,000 in 1928 to 112 in 1950. This compares favorably with the decline in tuberculosis mortality among American Indians from 354.6 per 100,000 in 1929 to 211.9 in 1945,[2] although it is still far from ideal.

### *Clinical Facilities*

At the Hospital of American Samoa two wards containing 42 beds are designated for the treatment of tuberculosis, and an additional ward of

The opinions and assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

*Presently in Forest Hills, New York.

23 beds is reserved for suspected tuberculosis cases and noncontagious forms of the disease. The Hospital is equipped with usual roentgenographic instruments excluding tomographic. The laboratory was able to perform all usual clinical examinations except cultures of the sputum and guinea pig innoculations. Reliance had to be placed therefore on examinations of the concentrated sputum. Specific therapies included adequate diet and bedrest, artificial pneumothorax and pneumoperitoneum, phrenic crush, and streptomycin. Surgical treatment for extrapulmonary tuberculosis was available, but there were no facilities for "chest surgery" such as thoracoplasty.

### *The Patients*

This series of 100 cases of tuberculosis was accumulated as follows: To 25 patients in hospital at the beginning of the study there were added the next 75 admitted because of tuberculosis. Strictly speaking, therefore, it does not represent 100 consecutive hospital admissions. The cases were chosen in this fashion since the number (100) is large enough to be representative, and since all were treated according to one general plan under the same supervision. The advantages of this selection are considered to outweigh the disadvantages, which are obvious, namely that some previous successes and failures are not included. It is believed that the time of observation was long enough to justify the drawing of tentative conclusions. The desirability of a five-year follow-up are conceded, and such may later be attempted.

### *Types of Tuberculous Disease*

Tuberculosis is a systemic disease whose principal manifestations occur in one or more localities in the body. The types of clinical tuberculous disease encountered among hospital admissions (hospitalization is legally mandatory and seldom avoided) are set forth in Table I.

TABLE I
TYPES OF TUBERCULOUS DISEASE IN 100 SAMOAN PATIENTS

| Type | No. Cases | Males | Females | Average Age | Died | Quiescent | Remain In Hosp. |
|---|---|---|---|---|---|---|---|
| Pulmonary Primary | 7 | 2 | 5 | 3.3 yr. | 0 | 7 | 0 |
| Reinf. Min. | 7 | 4 | 3 | 26.9 | 0 | 6 | 1 |
| Reinf., Mod. Adv. | 28 | 12 | 16 | 30.5 | 5 | 12 | 11 |
| Reinf., Far Adv. | 23 | 9 | 14 | 28.4 | 7 | 0 | 16 |
| Lymphadenitis | 13 | 10 | 3 | 15.8 | 2 | 9 | 2 |
| Meningitis | 6 | 1 | 5 | 16.5 | 2 | 4 | 0 |
| Miliary | 5 | 2 | 3 | 10.0 | 5 | 0 | 0 |
| Pleurisy with Effusion | 6 | 5 | 1 | 29.3 | 1 | 5 | 0 |
| Osteitis | 2 | 1 | 1 | 25.5 | 0 | 2 | 0 |
| Nephritis | 1 | 1 | .. | 34.0 | 1 | 0 | 0 |
| Peritonitis | 2 | 1 | 1 | 8.0 | 1 | 1 | 0 |
| | 100 | 48 | 52 | 20.7 | 24 | 46 | 30 |

Notes: Number of Cases equals percentage.
Ages given as of time of hospital admission.
Autopsy control: Autopsies in 33.3 per cent fatal cases.

Tuberculosis of the lungs accounted for 65 per cent of the total number of cases. The percentage of lymphadenitis is somewhat larger than would be expected in continental practice, although it was found by the senior author to be 4.3 per cent of a series of 163 U. S. Naval patients. In these Samoan patients, it will be recalled that all ages, from infancy upward, are included. The distribution of the other types of extra-pulmonary tuberculosis is not considered to be unusual considering the age span. The extent of the reinfection type pulmonary tuberculosis cases is not unlike that of U. S. Naval cases.[3] There were no bizarre forms of tuberculosis encountered which did not readily fit into established classifications.

The conclusion may, therefore, be drawn that tuberculosis among Samoans presents no unique or remarkable clinical manifestations.

### *Results of Treatment*

1. *Primary Tuberculosis.* A diagnosis of primary pulmonary tuberculosis was established on the basis of positive tuberculin test plus appropriate roentgenographic findings. The seven patients ranged in age from seven months to eight years, with an average of 40.9 months. There were two boys and five girls. Treatment consisted primarily of hospitalization to minimize activity. Streptomycin was given to one marasmic infant (0.5 g. daily for 58 days) and to one with diffuse bronchogenic spread due to endogenous reinfection (0.25 g. daily for 40 days) with excellent results. All children recovered after an average hospitalization of 88.6 days. There was no observed relapse.

2. *Minimal Reinfection Disease.* Seven patients, four males and three females, from 13 to 57 years of age (average 26.9) had minimal reinfection type of pulmonary disease roentgenographically, with either positive sputum or positive tuberculin test. Five treated with bed rest alone and one borderline case who received artificial pneumothorax in addition, recovered uneventfully, after an average hospitalization of nine months. One boy of 17, discharged as quiescent, returned later with tuberculous fistula in ano (proved by biopsy) which was successfully treated by surgery and streptomycin. One girl aged 16 progressed to far advanced disease, and was still in hospital after one year despite artificial pneumoperitoneum and streptomycin. The immediate outcome was thus favorable in 85.7 per cent of cases.

3. *Moderately Advanced Reinfection Disease.* This was the largest group of pulmonary cases, 28 in number. There were 12 males and 16 females, aged from 16 to 67 years (average 30.5). Artificial pneumothorax was induced or attempted in 14, but was abandoned in favor of pneumoperitoneum in two and of phrenic crush in two because of unsatisfactory collapse. Pneumoperitoneum was employed initially in three. Six received streptomycin.

Of the 28, 12 became quiescent and five died. Eleven remained in hospital, six of whom were believed to have a favorable prognosis. The expected salvage rate is therefore about 60 per cent. This figure is undoubtedly optimistic, since it takes no account of possible future relapses.

4. *Far Advanced Reinfection Disease.* There were, unfortunately, 23

in whom far advanced disease was found on admission. This group included nine males and 14 females between the ages of 10 and 62 (average age 28.4). One, a boy of 10, had been previously treated for tuberculous polyserositis. Artificial pneumothorax was selected as the initial collapse therapy in five cases, to be supplanted by artificial pneumoperitoneum in three and by phrenic crush in one. Nine received pneumoperitoneum from the start, three with added phrenic crush. Streptomycin was employed in 17 cases.

No one of these patients reached a stage of quiescence by the time the period of observation ended, and seven had died. Of the 16 survivors, the prognosis was thought to be favorable for life in 11. There is accordingly a possibility (again undoubtedly optimistic) of salvage of about 40 per cent.

*Extrapulmonary Tuberculosis*

1. *Tuberculous Lymphadenitis.* Among 13 patients with scrofula, there were 10 males and three females, the youngest two, the oldest 37 years of age. The average age was 15.8 years. One adult was experiencing his fourth hospitalization for this condition, and another his second. The diagnostic criteria included positive tuberculin test as well as physical findings. One biopsy was performed, and there were four post-operative examinations of tissue.

Nine were discharged as quiescent. Two died, the one because of miliary spread, the other because of coincidental internal hydrocephalus, probably congenital. Average hospital stay in these 13 cases was 5.3 months. Two remain in hospital, a boy gravely ill with miliary disease and a girl of 23, well on the road to recovery despite diffuse lymphadenitis (including intraabdominal), pleurisy with effusion, peritonitis, and pregnancy. The expected salvage rate is therefore about 77 per cent.

Streptomycin was given to 11 patients because of draining sinus (five cases), miliary dissemination (two cases), and as a preoperative prophylactic (four cases). The dose was 0.5 to 1.0 grams daily for adults and adolescents, and 0.2 to 0.25 grams for small children, given for from 18 to 50 days. It was responsible for sinus closure in four patients. It checked miliary spread in one, but failed in two. Used as a pre-operative prophylactic, it appeared to prevent complications. In one case with generalized lymphadenopathy it was helpful. One with massive cervical lymphadenopathy alone received no benefit.

2. *Tuberculous Meningitis.* One male and five females were admitted because of tuberculous meningitis. The span of ages was from 18 months to 30 years, the average age 16.5. All received streptomycin intramuscularly and four intrathecally. The intramuscular daily dose was 1.0 grams for adults, 0.2 grams for children, the intrathecal dose 0.025 to 0.050 grams. The duration of intramuscular treatment was from 25 to 98 days. Four recovered, and two died. The patient who received 98 grams of the drug developed ataxia, which cleared slowly over a period of one year.

3. *Miliary Tuberculosis.* Five patients were found to have miliary disease on admission, two males and three females. The youngest was 18 months old, the oldest 22 years. Average age was 10 years. Four died,

despite streptomycin, in three cases, and the fifth, also streptomycin treated, was not expected to recover. Daily dose was 0.5 grams in an infant to 1.5 grams in an adult, given for from three to 137 days.

The total failure of treatment in these cases, as well as in all but one of the patients who developed miliary tuberculosis intercurrently, suggests inadequate dosage of streptomycin.

4. *Pleurisy with Effusion.* Five males and one female from 16 to 48 years (average 29.3), had pleurisy with effusion assumed to be tuberculous because of clinical findings, type of fluid aspirated, and positive tuberculin test. After an average hospital stay of 9.1 months, five apparently recovered, and the sixth was permitted to go home for supervised rest. This last, a man of 48, returned later with carcinoma of the prostate and an increase of pleural effusion. Prostatectomy was mandatory and successful, except that the supra-pubic fistula developed tuberculous granulations and did not heal despite streptomycin treatment. He died suddenly several weeks post-operatively. Autopsy showed tuberculosis of adrenals, kidneys, the vesical fistula, and extensive caseo-cavernous disease of the left lung (concealed by the fluid from roentgenographic visualization).

5. *Tuberculous Osteitis.* A youth of 16 was treated successfully by spine fusion and streptomycin (0.5 grams daily for 45 days) for Potts' disease of the 10th dorsal vertebra with visible deformity and sphincteric disturbance. A woman of 35 had chronic tuberculous osteomyelitis of the distal extremity of the right middle metacarpal bone, with sinus formation and scrofuloderma, of five years duration. The entire process was halted abruptly by 14 grams of streptomycin in the same number of days. Both patients were well over one year after treatment.

6. *Tuberculosis of Kidneys.* A man of 34 died soon after admission for bilateral caseo-cavernous renal tuberculosis with cystitis and peritonitis. Autopsy revealed in addition a minimal lesion of the apex of the left lung.

7. *Tuberculous Peritonitis.* A girl of nine died from tuberculous peritonitis. A boy of seven recovered. Both received streptomycin (the girl 1.0 grams daily for 47 days, the boy 0.5 grams daily for 42 days). The boy also had laparotomy performed as a therapeutic measure.

## *Comment*

At the risk of repetition it is considered appropriate to comment further on collapse therapy and on the use of streptomycin in these cases.

1. *Collapse Therapy.* There is no set of rules to follow regarding collapse therapy in pulmonary tuberculosis. The decision in each case as to the desirability and form of treatment to be used must be based upon the nature of the lesions, the stage of the disease, and the general condition of the patient. Often there is no indication for collapse therapy, or at least there is none at the particular time, or delay for a period of a month or two is justified in the hope that some thin-walled cavities will close spontaneously. This last occurred in three of our cases.

In all, some form of collapse therapy was employed in 33 (56.8 per cent) of the 58 cases of reinfection type pulmonary tuberculosis.

The reasons for non-employment were: Not considered indicating (in-

cluding five minimal cases) 18 cases; too old, three; in terminal state, two cases; procrastination until too late, one. In retrospect, collapse might have averted or postponed a fatal outcome in three of these individuals.

When the decision to use collapse therapy was reached in any case, artificial pneumothorax was considered to be the treatment of choice if applicable.[4] There were 20 patients among the 33 collapsed patients considered to be suited to this treatment. Successful collapse was achieved in only 13 of them, with cavity closure in nine. On the other hand, pneumothorax had to be abandoned in seven cases because of adhesions or other difficulties in favor of pneumoperitoneum (five cases) and phrenic crush (two cases). Pleural effusions, some serious enough to demand discontinuance of treatment sooner than was desired occurred in 10 cases of the 13 successfully collapsed (77.2 per cent). Four of these were probably due to overenthusiastic inflations, but the reason for the other six was not apparent.

Artificial pneumoperitoneum, induced as the primary treatment in 13 cases (because of bilaterality of disease, fear of empyema, or probability of adhesions, and after pneumothorax failure in five), was technically easy, free of complications, and reasonably effective. Phrenic crush was added in three cases. The average elevation of the diaphragm on the higher side was 2.8 cm. This figure suggests overcaution. Cavity closure occurred in but one case during observation, but diminution of the cavitary area was noted in six patients. Since pneumoperitoneum was usually given to the patients having more extensive lesions, this lower rate of cavity closure is not surprising.

In general, in these particular patients, artificial pneumothorax was a more successful treatment from the point of view of cavity closure than was pneumoperitoneum, but was attended by many more difficulties in practice. It may be noted that in patients initially treated subsequent to this particular series of cases there was a larger proportion of initial pneumoperitoneum than of pneumothorax.

Phrenic crush was used only after pneumothorax failure or to reinforce pneumoperitoneum. It was conspicuously successful anatomically and clinically in only one of the latter group.

2. *Streptomycin.* The use of streptomycin in these cases was based upon the assumption that streptomycin may be lifesaving, and that therefore it should be withheld unless life itself was directly threatened. The objective therapeutically was, consequently, always the limited objective of meeting some emergency, and success or failure must be judged according to whether or not the drug enabled the patient to meet the particular emergency. In tuberculous meningitis or in miliary tuberculosis, naturally, the objective and the result are either all or none.

The basic dosage employed was that of Dickman,[5] namely 0.5 grams per day. In the case of children this was reduced, or in the case of adults, was increased when the 0.5 grams dosage appeared ineffective or when the situation was critical. The briefest period over which it was used was three days, the longest 194. All told, 50 patients received streptomycin at one time or another. The largest total dose administered was 194 grams.

Toxic effects were noted in two, one with ataxia (mentioned above) and one of urticarial dermatitis.

The use of streptomycin in extra-pulmonary tuberculosis and the results achieved have been sufficiently described above. In pulmonary cases the reasons for use and the results accomplished were as follows:

TABLE II
RESULTS OF STREPTOMYCIN TREATMENT IN PULMONARY TUBERCULOSIS

| Reason for use | No. Cases | Result Successful |
|---|---|---|
| Pneumonic Phthisis | 2 | 2 |
| Bronchogenic Spread | 8 | 5 |
| Miliary Spread | 6 | 1 |
| Toxemia | 3 | 2 |
| Intercurrent Meningitis | 3 | 2 |
| Intercurrent Peritonitis | 1 | 1 |
| Intercurrent Laryngitis | 1 | 1 |
| | 24 | 14 (59 per cent) |

If the three cases of intercurrent meningitis be added to the six admitted with that diagnosis, the results of streptomycin treatment may be considered to have saved life in six cases (two-thirds of the total). Putting together all the miliary cases, both original and intercurrent, the total number was seven, and the outcome favorable in but one.

Finally, a general appraisal of the immediate therapeutic results in the 100 Samoan patients is appropriate.

Table I indicates that the mortality rate during the two years of study was 24 per cent. On the other hand, 46 per cent of the patients achieved a state of quiescence during that time. There remained 30 (30 per cent) in hospital, among whom the prognosis was considered to be good in 18. Assuming this favorable prognosis to be accurate, eventual recovery could be expected in 64 per cent of the cases. With continuing improvement in the control and treatment of tuberculosis among the Samoans, there is no reason to doubt that the disease will continue to recede in importance in the islands.

## SUMMARY

1. A study of 100 cases of tuberculosis among Samoans (Polynesians) is reported.
2. Environmental data, notes on control measures, diagnostic and treatment facilities are outlined.
3. The types of tuberculous disease encountered are enumerated. No unusual pattern was observed.
4. The types of treatment employed and the results obtained during the two year period are detailed.
5. Artificial pneumoperitoneum was found to be generally more practicable than artificial pneumothorax in the treatment of pulmonary cases.
6. Reasons are indicated for optimism regarding the future course of the disease in the islands.

RESUMEN

1. Se relata el estudio de cien casos de tuberculosis entre los samoanos (polinesios).

2. Se describen los datos del ambiente, medidas profilacticas y las posibilidades diagnósticas y del tratamiento.

3. Se enumeran las formas encontradas de enfermedad tuberculosa. No se encontró formas inusitadas.

4. Se detallan las formas tratamiento usado y los resultados obtenidos durante el período de dos años.

5. El neumoperitoneo artificial, se encontró en general, más practicable que el neumotórax en el tratamiento de la tuberculosis pulmonar.

6. Se señalan las razones para ser optimista respecto de la evolución ulterior de la enfermedad en las islas.

RESUME

1. Les auteurs rapportent l'étude de 100 cas de tuberculose chez les Samoans (Polynésiens).

2. Ils esquissent les éléments du milieu social et les caractères des mesures de contrôle, de diagnostic, et des facilités de traitement.

3. Ils énumèrent les variétés d'affections tuberculeuses qu'ils ont rencontrées. Aucun type inhabituel ne fut observé.

4. Ils décrivent en détail les différents modes de traitement utilisé, et les résultats obtenus pendant une période de deux ans.

5. Le pneumopéritoine se montra plus indiqué généralement que le pneumothorax artificiel dans le traitement des cas de tuberculose.

6. Les auteurs donnent les raisons de leur optimisme en ce qui concerne l'évolution future de la maladie dans les îles.

REFERENCES

1 Buck, P. H.: "Vikings of the Sunrise," *Frederick A. Stokes Co., New York 1938*, p. 16.

2 Reifel, A.: "Tuberculosis Among Indians of the United States," *Dis. Chest*, 16: 234, 1949.

3 Gray, J. A. C.: "Pulmonary Tuberculosis: Experiences in a Naval Hospital," *U. S. Naval Medical Bulletin*, 48:921, 1948.

4 Cohen, A. J.: "Forty Years Experience with Artificial Pneumothorax," *Dis. Chest*, 17:74, 1950.

5 Dickman, R. W.: "One Half Gram of Streptomycin in the Treatment of Pulmonary and Extrapulmonary Tuberculosis," *Dis. Chest*, 15:422, 1949.

# Bronchiectasis: Practical Consideration of Cure, Treatment and Prognosis

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It is the purpose of this paper to point out that symptomatic bronchiectasis results in death from infection, hemorrhage and pulmonary insufficiency; and that in approximately one-half of the cases, cure is possible and desirable by segmental resection of the diseased areas.

## *Anatomy*

The lungs are formed of units known as bronchopulmonary segments. Each is a cone of tissue with its own bronchus and blood supply.[5] Two or more may be grouped together as a lobe, but individual segments of any lobe may be diseased without involvement of the others, and individual segments may be removed without damage to other segments of a lobe.[6] This concept is of particular importance in the consideration of bronchiectasis, because this disease characteristically affects *some* segments of *several* lobes.

## *Pulmonary Function*

We do not have unlimited pulmonary function. Physical activity of the young is curtailed by limitations in respiratory and cardiac function. As the degenerations of age occur, the impairment of cardiac and pulmonary function are additive and mutually embarrassing. A damaged heart might sputter along if the lungs are normal—but fail completely should there be pulmonary limitation as well.

## *Pathologic Physiology*

The air we breathe contains great quantities of dust, bacteria, and foreign material. Were there no mechanism for removal of this, the bronchi would, in time, become completely filled. Fortunately, the bronchial wall forms mucus to dissolve some of the foreign matter, has a ciliary brushing mechanism to move the mucus proximally, and in addition, the bronchial cough explodes larger particles upward and out of the bronchial tree.

The bronchiectatic change results in a thickened wall, destruction of some of the mucus glands, and of the cilia. Other factors which interfere with drainage are pleural thickening, enlarged hilar nodes, deformation of the chest wall, or immobilization of the diaphragm by pregnancy. In the upper lobes, the force of gravity is usually effective in facilitating bronchial drainage, but in the dependent segments, gravity acts unfavorably and stagnation occurs. Inhaled bacteria are not promptly eliminated, but grow in the accumulated secretion and infection results. The quantity of purulent material may become great, so that the usual ineffective cough

of the bronchiectatic cannot expel it at one time. Coughing is paroxysmal and mixed with deep inspirations which suck pus and bacteria into normal pulmonary segments.

By this means, severe clinical attacks of pneumonitis in otherwise normal lung tissue may be produced, but far more often, the degree of pneumonitis and/or atelectasis is so slight that early fatigue, lassitude and malaise may be the only symptoms. Each such process results in some scar, and after 20 or 30 years have passed, it is frequent to find widespread secondary pulmonary fibrosis and emphysema and markedly limited respiratory function. In this state of borderline pulmonary capacity, any thoracic disease, such as pneumonia, fractured ribs, cardiac decompensation, etc., may result in death.

### *Diagnosis*

A diagnosis of bronchiectasis can only be proved or disproven by a complete bronchogram; i.e., one with filling of all 18 segmental bronchi.

### *Significance of Demonstrated Bronchiectasis*

The extent and degree of bronchiectatic change are less significant than the presence or absence of symptoms. A patient with widespread bronchiectasis may be relatively asymptomatic; whereas one single bronchiectatic segment which is not well-drained may result in recurrent pneumonia, hemorrhage, empyema, or even brain abscess.

### *Complications*

Infection. Prior to the development of modern chemotherapy, infection was the usual direct cause of death in bronchiectasis.

Perry and King,[4] in 1940, published a follow-up study on 400 patients with bronchiectasis. Sixty-nine per cent developed symptoms in the first two decades of life. Of 96 nonsurgical cases who developed bronchiectasis before the 10th year, 62 were dead in less than 20 years from the onset. Only 9 (9.4 per cent) lived 30 or more years. The mortality was almost identical in those with commencement in the second decade. When one realizes the early beginning of the disease in most patients and that most die in less than 20 years, it becomes apparent that those with symptomatic, untreated bronchiectasis usually are dead before they are 40.

Bradshaw and Clerf,[1] in 1941, reviewed 171 patients with untreated bronchiectasis seen originally between 1925-35. Fifty-nine (34.5 per cent) died from bronchiectasis or its complications up to the time of report. The average duration of life in those who died was 13½ years.

With present day antibiotics, infections occur but are generally easily controlled. Empyema and brain abscess are much more uncommon than formerly. They still occur, however, and brain abscess especially may result from subclinical infection.

Arthritis is common, and even minor arthritic symptoms should be viewed as an indication that smoldering infection is present.

*Hemorrhage*

Scannell[7] in 1950 reported a 10 year follow-up on bronchiectatic patients who, at the Massachusetts General Hospital, had indications for surgical resection, but surgery was not performed. He found that 11 were well, but that four had died from massive pulmonary hemorrhage and one from "general decay." It is important to realize that fatal pulmonary hemorrhage is a common termination in bronchiectasis.

Pulmonary insufficiency. Although, with chemotherapy and antibiotics, even severe infections can be controlled and far less often result directly in death, the scarring which results eventually leads to crippling and premature demise from pulmonary insufficiency.

In this respect, it is interesting to compare diabetes mellitus and bronchiectasis. Joslin[3] states, "Total *absence* of vascular disease occurred infrequently after 20 years of diabetes. . . ." When diabetic control is not perfect, the occurrence of atherosclerotic change is early and severe. The usual cause of death in diabetes mellitus of long duration is vascular change in the brain, heart or kidney. In diabetes too, because of antibiotics, infection is no longer the customary cause of death. If there were a surgical operation which would cure diabetes mellitus, would that not be greatly preferable from standpoints of daily well-being, economics, and ultimate prognosis than the present day management with substitution insulin? So too in symptomatic bronchiectasis of limited extent, surgical cure is more economical, offers a longer prognosis, and provides a healthy, symptom-free daily life. Present day surgical mortality is 0.4 per cent.[2]

Approximately 50 per cent of bronchiectasis cases are not surgical. Symptomatic cases where nearly all segments are involved are beyond surgical cure for obvious reasons. Infrequent mild hemoptyses, without other symptoms, require nothing more than reassurance. Anatomical bronchiectasis in a segment or segments which are well-drained and thus do not become infected, or in which infections are mild and infrequent, and *where the intervals are completely free from evidence of infection* does not require more than symptomatic therapy. But should there be fatigue, chronic cough, increased sputum production, arthritis, or general malaise in the interim, low-grade chronic infection is present, and in such a situation, surgery is indicated.

## SUMMARY

Surgical Bronchiectasis is symptomatic disease significantly affecting less than 12 bronchopulmonary segments, where the remaining segments have adequate functional capacity. This emphasizes the factor of time. In surgical bronchiectasis, cure can be obtained by surgical removal, if done before secondary changes are produced in nonbronchiectatic segments. So-called conservative treatment, in such cases, may result in partial control of symptoms and infections, but, nevertheless recurrent minor inflammations over the years finally produce secondary fibrosis and emphysema and early death from pulmonary insufficiency.

## RESUMEN

La bronquiectasia quirúrgica, es una enfermedad que afecta significativamente menos de 12 segmentos, en tanto que los segmentos restantes, tienen adecuada capacidad funcional. Esto acentúa la importancia del factor tiempo.

En la bronquiectasia de tipo quirúrgico, la curación puede obtenerse por la excisión quirúrgica si se lleva a cabo antes de que aparezcan cambios secundarios en los segmentos no bronquiectásicos. El llamado tratamiento conservador en tales casos, puede obtener un control parcial de los síntomas y de la infección pero sin embargo, las inflamaciones de menor cuantía, pero recurrentes por años, producen fibrosis secundaria y enfisema y muerte temprana o por insuficiencia pulmonar.



## RESUME

On peut considérer comme chirurgicales les bronchiectasies qui atteignent incontestablement moins de douze segments bronchopulmonaires. Les autres segments doivent conserver une valeur fonctionnelle suffisante. Ceci met l'accent sur l'importance du facteur "temps". Dans la bronchectasie "chirurgicale", la guérison peut être obtenue par exérèse, si celle-ci est réalisée avant que des altérations secondaires ne se soient produites dans les segments non bronchectasiques. Dans de tels cas, le traitement conservateur peut amener une guérison partielle des symptômes et de l'infection. Toutefois, avec les années, de petites actions récurrentes produisent finalement une fibrose secondaire avec emphysème, et entrainent une mort prématurée par insuffisance pulmonaire.


## REFERENCES


1 Bradshaw, H. H., Putney, J. F. and Clerf, L. H.: "Fate of Patients with Untreated Bronchiectasis," *J.A.M.A.*, 116:2561, 1941.

2 Forsee, J. H. and Klinger, P. E. J.: "Lobectomy for Bronchiectasis," *Annals of Surg.*, 137:74, 1953.

3 Joslin, E. T.: "Treatment of Diabetes Mellitus," *Lea & Febiger*, 1952.

4 Perry, K. M. A. and King, D. S.: "Bronchiectasis: Study of Prognosis Based on Follow-up of 400 Patients," *Am. Rev. Tubere.*, 41:531, 1940.

5 Ramsay, B. H.: "The Anatomic Guide to the Intersegmental Plane," *Surgery*, 25: 533, 1949.

6 Ramsay, B. H.: "Conservation of Tissue and Function in Pulmonary Resection—The Technique of the Anatomical Separation of Segments," *Calif. Med.*, 76:333, 1952.

7 Scannell, J. G.: "Discussion of paper by Drs. Rosemond, Burnett and Humphrey-Long," (p. 439). *J. Thor. Surg.*, 22:448, 1951.

THE WHITE HOUSE

WASHINGTON

July 23, 1954

Dear Dr. Greer:

I am delighted to send greetings to the Third International Congress on Diseases of the Chest.

The exchange of information at international conferences such as this leads inevitably to the betterment of men and women everywhere. This scientific assembly is also proof that people of good faith can transcend geographic boundaries and distinctions of race, creed and color in common dedication to a humanitarian cause.

To all of you gathering in Barcelona, I extend best wishes for an enjoyable and productive meeting.

Sincerely,

Dwight D. Eisenhower

Dr. Alvis E. Greer
Past President
American College of Chest Physicians
112 East Chestnut Street
Chicago 11, Illinois

*Greetings from Dwight D. Eisenhower, President of The United States of America to the delegates attending the Third International Congress on Diseases of the Chest, sponsored by the Council on International Affairs American College of Chest Physicians, and the government of Spain at Barcelona, Spain, October 4-8, 1954.*

# Interim Session

## AMERICAN COLLEGE OF CHEST PHYSICIANS

The Interim Session of the College will be held November 28 and 29, 1954 at the Delano Hotel, Miami Beach, Florida. On Sunday, November 28, the Florida Chapter of the College will sponsor a scientific program, and on Monday, November 29, the Executive Council, the Board of Regents and the Board of Governors will hold their semi-annual meetings. Examinations for Fellowship in the College will be conducted at the Delano Hotel on Saturday, November 27. At the close of the Interim Session, delegates are invited to attend the meeting of the Cuban Chapter of the College to be held in Havana, December 1. The Clinical Meeting of the American Medical Association will be held in Miami Beach, November 30-December 3.

The Committee on Scientific Program, under the direction of Dr. Alexander Libow of Miami Beach, Chairman, and Dr. Henry C. Sweany, Tampa, Vice-Chairman, has arranged the following program:

### SUNDAY, NOVEMBER 28

#### Morning Session

DeWitt C. Daughtry, President, Florida Chapter, American College of Chest Physicians, Miami, Chairman

Jack Reiss, Secretary-Treasurer, Florida Chapter, American College of Chest Physicians, Coral Gables, Co-Chairman

9:00 a.m. "Physiological Aspects of Lung Cancer"
Seymour M. Farber and Roger H. L. Wilson, San Francisco, California

"Surgical Treatment of Coronary Artery Disease"
Charles P. Bailey, Philadelphia, Pennsylvania

"The Effect of Prolonged Exercise on Heart and Lungs"
Burgess L. Gordon, Philadelphia, Pennsylvania

"Chronic Irritants Versus Span of Life and Early Diagnosis in Bronchogenic Carcinoma"
George G. Ornstein and Lawrence Lercher, New York, New York

"Pulmonary Findings Associated with Lupus Erythematosis"
Herman J. Moersch, Rochester, Minnesota

12:00 p.m. Round Table Luncheons

1) "Chemotherapy in Diseases of the Chest"
Benjamin L. Brock, Orlando, Florida; Maurice Campagna, New Orleans, Louisiana; Harold G. Trimble, Oakland, California
*Moderator:* James H. Stygall, Indianapolis, Indiana

2) "Cancer of the Lung"
Duane M. Carr, Memphis, Tennessee; Alfred Goldman, Beverly Hills, California; Henry J. Stanford, Tucson, Arizona
*Moderator:* David H. Waterman, Knoxville, Tennessee

3) "Pulmonary Function"
Albert H. Andrews, Jr., Chicago, Illinois; Ross C. Kory, Milwaukee, Wisconsin; Maurice S. Segal, Boston, Massachusetts
*Moderator:* Edwin R. Levine, Chicago, Illinois

#### Afternoon Session

2:00 p.m. Hawley L. Seiler, Vice President, Florida Chapter, American College of Chest Physicians, Tampa, Chairman

Nathaniel M. Levin, Immediate Past-President, Florida Chapter, American College of Chest Physicians, Miami, Co-Chairman

2:00 p.m. "Cancer of the Lung in Mass X-ray Survey"
Alfred Goldman, Beverly Hills, California

"Clinical Features of Airspace Abnormalities of the Lung"
Edgar Mayer, New York, New York

"Tuberculosis Among Nurses"
Jay Arthur Myers, Minneapolis, Minnesota

*Panel Discussion:* "Modern Management of Pulmonary Tuberculosis"
James S. Edlin, New York, New York; Hollis E. Johnson, Nashville, Tennessee; Henry C. Sweany, Tampa, Florida; David Ulmar, New York, New York

*Moderator:* Alvis E. Greer, Houston, Texas

**Evening Session**

6:30 p.m. Cocktail Party
By courtesy of the Florida Chapter,
American College of Chest Physicians

7:00 p.m. Dinner
Alexander Libow, Chairman, Scientific Program Committee,
Miami Beach, Florida, Toastmaster

*Guest Speaker:* William A. Hudson, President, American College of Chest Physicians, Detroit, Michigan

8:30 p.m. "Diagnostic and Treament Conference"
DeWitt C. Daughtry, Miami, Florida; Edwin R. Levine, Chicago, Illinois; Hawley L. Seiler, Tampa, Florida; Clarence M. Sharp, Jacksonville, Florida.

*Moderator:* M. Jay Flipse, Miami, Florida

**MONDAY, NOVEMBER 29**

**Executive Sessions**

8:00 a.m. Meeting of the Executive Council

10:30 a.m. Joint meeting, Board of Regents and Board of Governors

12:00 noon Luncheon, Board of Regents and Board of Governors

2:00 p.m. Semi-Annual Meeting, Board of Regents

**TUESDAY, NOVEMBER 30—Clinical Meeting, American Medical Association**

**Section on Diseases of the Chest**
Jack Reiss, Coral Gables, Florida,
Chairman, Chest Section Committee

9:00 a.m. Panel on Tuberculosis "Modern Concepts in the Chemotherapy of Pulmonary Tuberculosis"
Oscar Auerbach, East Orange, New Jersey; H. Corwin Hinshaw, San Francisco, California; Carl W. Temple, Denver, Colorado; William B. Tucker, Durham, North Carolina

10:00 a.m. "Acute Pulmonary Diseases"
John H. Seabury, New Orleans, Louisiana

10:30 a.m. Visit Exhibits

11:00 a.m. "Treatment of Chronic Pulmonary Diseases and Carcinoma of the Lungs"
Alvis E. Greer, Houston, Texas

11:30 a.m. Visit Exhibits

12:00 noon "Recent Advances in the Management of Chronic Pulmonary Emphysema"

Maurice S. Segal, Boston, Massachusetts

All sessions will be held at the Delano Hotel in Miami Beach. Reservations for the round table luncheon discussions may be made through the Executive Offices of the College in Chicago. Requests for reservations must be accompanied by remittance in the amount of $3.00 for each luncheon. Please indicate choice by number.

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## CUBAN CHAPTER MEETING

**DECEMBER 1**

Official Welcome—Antonio Navarrete, Havana, Regent for Cuba, American College of Chest Physicians

Report of the Third International Congress on Diseases of the Chest sponsored by the Council on International Affairs, American College of Chest Physicians

William A. Hudson, Detroit, Michigan, President

"What Are the Prospects of Cure of Cancer of the Lung by Surgery"

Herman J. Moersch, Rochester, Minnesota
*Discussor:* Leopoldo Araujo, Havana

"The Selection and Management of Patients with Thoracic Diseases for Air Travel"

Burgess L. Gordon, Philadelphia, Pennsylvania
*Discussor:* R. Covas, Havana

"Pulmonary Tuberculosis Therapy—A Study of Ten Cases by 100 Participating Physicians"

Harold G. Trimble, Oakland, California
*Discussor:* Ricardo Sanchez Acosta, Havana

"Unsolved Problems in Specific Drug Therapy of Tuberculosis"

H. Corwin Hinshaw, San Francisco, California
*Discussor:* René Garcia Mendoza, Havana

"Surgery of Coronary Artery Disease"

Charles P. Bailey, Philadelphia, Pennsylvania
*Discussor:* Antonio Rodríguez Diaz, Havana, Cuba

# College Chapter News

## SOUTHERN CHAPTER

The 11th annual meeting of the Southern Chapter, which includes the 16 southern states and the District of Columbia, will be held in conjunction with the meeting of the Southern Medical Association, at the Sheraton Hotel, St. Louis, Missouri, November 7-8. The Committee on Scientific Program, under the chairmanship of Dr. Alfred Goldman, St. Louis, has arranged the following program:

**NOVEMBER 7**

**Morning Session**

9:00 a.m. Registration

9:30 a.m. Scientific session

John H. Seabury, New Orleans, Louisiana, Chairman, Medical Section, presiding

"Lipoid Granuloma of the Lung of Exogenous Origin"
Howard A. Buechner and Lawrence H. Strug, New Orleans, La.

"Some Factors Affecting Isolation of Tubercle Bacilli from Patients Receiving Long-term Chemotherapy"
Thomas C. Black and Edith L. Duerr, Ph.D., Alexandria, Louisiana

"The Half-Second Expiratory Capacity Test: A Convenient Method of Determining the Nature and Extent of Ventilatory Insufficiency in Various Pulmonary Disorders"
William F. Miller, Robert J. Johnson, Jr., Nancy Wu, and Russell M. Horn, Dallas, Texas

"Tuberculin Testing"
Daniel Jackson, Houston, Texas

12:00 p.m. Round Table Luncheon Meeting—"Angina Pectoris and Coronary Thrombosis"

*Moderator:* Samuel B. Grant

*Panel:* James G. Janney, Jr., Edward Massie, and Arthur E. Strauss, St. Louis, Missouri

**Afternoon Session**

2:00 p.m. Charles R. Kessler, Birmingham, Alabama, Chairman, Surgical Section, presiding

"Surgical Treatment of Bullous Emphysema"
Harry E. Walkup and Mark W. Wolcott, Oteen, North Carolina

"Mediastinal and Para-Mediastinal Tumors"
DeWitt C. Daughtry, Miami, Florida

"Resection for Tuberculosis; 500 Cases"
F. H. Cole, Memphis, Tennessee

"Present Status of Cardiovascular Surgery"
Osler A. Abbott, Atlanta, Georgia

6:30 p.m. Social Hour, Sheraton Hotel

7:30 p.m. President's Banquet
Duane M. Carr, Memphis, Tennessee, Toastmaster
*Presidential Address:* John S. Harter, Louisville, Kentucky

9:00 p.m. "X-ray Conference"
William B. Seaman, Associate Professor of Radiology, Washington University School of Medicine, St. Louis

**NOVEMBER 8**

**Morning Session**

George R. Hodell, Houston, Texas, presiding

"The Effect of Aminophylline on the Heart and Lungs of Emphysemateous Patients"
Herbert C. Sweet, St. Louis, Missouri

"Biopsy in the Diagnosis of Pleural and Pericardial Effusion"
Sol Katz, George F. McCormick, and Nicholas Cotsonas, Washington, D. C.

"Pneumoconiosis in the Soft Coal Miner"
Louis L. Friedman, Birmingham, Alabama

12:00 p.m. Business Meeting

8:15 p.m. Paul A. Turner Lecture
"The Effect of Treatment of Tuberculosis on the Bacteriology and Pathology of the Disease"
Henry C. Sweany, Chief Medical Director, Florida Tuberculosis Board, Tampa, Florida

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## INDIANA CHAPTER

The annual meeting of the Indiana Chapter will take place in Indianapolis on October 26, at the time of the meeting of the Indiana State Medical Association. Dr. Andrew Offutt, Commissioner of the Indiana State Board of Health will speak on "Management of Recalcitrant Tuberculous Patients" which will be followed by an x-ray conference. Following lunch, the chapter will hold a business session in conjunction with the tuberculosis committee of the state medical association.

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## PACIFIC NORTHWEST CHAPTER

The Pacific Northwest Chapter, representing Oregon, Washington, Idaho, Montana, and British Columbia, will meet jointly with the American Trudeau Society chapter in Portland, Oregon, November 12 and 13. The scientific sessions will take place at the University of Oregon Medical School Library, and a dinner, scheduled for November 12, will be held at the Multnomah Hotel. Dr. Hurley L. Motley, Los Angeles, California, will be guest speaker and will talk on "Clinical Application of Pulmonary Function Studies" and "Recent Advances in Inhalation Therapy." Tuberculosis control officers of the northwest states and British Columbia will participate in a panel on "Communicability of Tuberculosis in Relation to Quarantine." An x-ray conference concerning difficult problems in tuberculosis management will also be presented, in addition to papers on angiocardiography, indications for aortic valve surgery, and roentgen therapy for interthoracic neoplasms.

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## PUERTO RICAN CHAPTER

A meeting of the Puerto Rican Chapter was held in Ponce, August 29. Speakers were Drs. J. J. de Lara, Francisco C. Porrata, Donald Babb, and Jaime Costas Durieux. Dr. J. Marchand presented motion pictures.

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## NORTHERN INDIA CHAPTER

Fellows and members of the College in the northern area of India met at the V. J. Hospital, Amritsar, May 9 to form the Northern India Chapter of the College. Dr. S. S. Anand of Amritsar was elected President of the chapter, and Dr. Khushdeva Singh, Patiala, was elected Secretary. A second meeting of the chapter is planned for the winter.

## NEWLY ELECTED OFFICERS

### NORTHERN CHAPTER, SOUTH AFRICA

J. K. Bremer, Pretoria, President
A. Rabinowitz, Johannesburg, Vice-President
L. D. Erasmus, Pretoria, Secretary-Treasurer

### MINNESOTA CHAPTER

Russell H. Frost, Oak Terrace, President
M. M. Williams, Ah-gwah-ching, Vice-President
B. J. Terrill, Nopeming, Secretary-Treasurer

### PENNSYLVANIA CHAPTER

Nathan Heiligman, Allentown, President
George Spencer, Pittsburgh, Vice-President
John V. Foster, Harrisburg, Secretary-Treasurer (re-elected)

### MICHIGAN CHAPTER

Forest D. Dodrill, Detroit, President
W. H. Barron, Detroit, Vice-President
Kenneth A. Wood, Detroit, Secretary-Treasurer

### WEST BENGAL (INDIA) CHAPTER

S. N. Sarbadhikary, Calcutta, President
P. K. Sen, Calcutta, Vice-President
P. K. Ghosh, Calcutta, Honorary Secretary-Treasurer

### VENEZUELA CHAPTER

In honor of the visit of Dr. Chevalier L. Jackson and Dr. Charles M. Norris, of Philadelphia, members of the College in Venezuela arranged a breakfast meeting in Caracas recently. Pictured above are (seated) Drs. Raul Soules Baldo, Jose Ignacio Baldo, Chevalier L. Jackson, Julio Criollo Rivas and Charles M. Norris. Standing are: Drs. Rafael Fernandez Ruiz, Jorge Echeverria Criollo, Alejandro Principe, Angel Larralde, Victor Gimenez, Cesar Rodrigues, Galdino Tattoni, Ladislao Pollack, Victor Yespica, Rogelio Valladares and Juan Delgado Blanco.

Dr. Harold G. Trimble, Oakland, California, Chairman of the Committee on Non-Surgical Collapse Therapy, was awarded the fourth Varrier-Jones Memorial Medal on the occasion of his lecture in London at Manson House, May 14, in memory of Sir Pendril Varrier-Jones, the founder of Papworth Village, the world famous industrial colony for the tuberculous, near London. The presentation was made by Dr. Richard R. Trail, Medical Director of Papworth and Governor of the College for Greater London. Sir Robert Young, C.B.E., presided and introduced Dr. Trimble, who spoke on "Current Treatment of Tuberculosis in the United States." The material for this lecture was obtained from the report of the Committee on Non-Surgical Collapse Therapy of the College. This committee studied the replies of 100 clinicians in the United States, all members of the College, as to their treatment of 10 routine cases of pulmonary tuberculosis.

While on the Continent, Dr. Trimble and Dr. Maurice Gilbert, Geneva, Governor of the College for Switzerland, represented the College at the Seventh Assembly of the World Health Organization, of which the College is an affiliated voluntary society. At a meeting of the Medical Society of Leysin, Switzerland, Dr. Trimble was guest speaker.

At the annual meeting of the Southwest German Tuberculosis Association in Wilbad, at which Dr. L. Rickmann, a Fellow of the College, presided, Dr. Trimble spoke on "The Medical Aspects" and Dr. Gerald Crenshaw, of Oakland, California, spoke on "The Surgical Aspects of Treatment of Tuberculosis in the United States." Dr. Attilio Omodei Zorino, Rome, Governor of the College for Northern Italy, presented a paper on "Combined Antibiotic Therapy of Pulmonary Tuberculosis" on the same program.

Dr. Richard R. Trail, London, England (right) awarding the Varrier-Jones Memorial Medal to Dr. Harold Guyon Trimble, Oakland, California.

# College News Notes

**Major General Harry G. Armstrong,** The Surgeon General of the United States Air Force, received a gold medal from the government of Chile for his "valuable services to the Chilean Air Force and to all humanity" as the author of "Principles and Practice of Aviation Medicine" and for his assistance in providing training to Chilean students at the U.S.A.F. School of Aviation Medicine.

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**Dr. Samuel Cohen,** Jersey City, New Jersey, has been appointed Director of Medicine at the B. S. Pollak Hospital for Chest Diseases. Dr. Cohen was formerly assistant to the medical director and chief of medical division 2 at the hospital.

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**Dr. Alfred D. Dennison, Jr.,** formerly of Maplewood, New Jersey, has joined the staff for Clinical Research at the Lilly Laboratory in Indianapolis, Indiana.

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**Dr. Burton L. Zohman,** Brooklyn, New York, Associate Clinical Professor of Medicine, State University of New York College of Medicine, addressed the American College of Cardiology meeting in Chicago on "The Immediate Prognosis of Acute Myocardial Infarction."

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**Dr. Arthur J. Vorwald,** formerly Director of the Saranac Laboratory, Trudeau, New York, has been appointed first professor of occupational medicine and Director of the Institute of Occupational Medicine at Wayne University, Detroit, Michigan.

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**Dr. Gordon A. Diddy,** formerly of Fresno, California, has been appointed supervisor of general tuberculosis activities for Fresno County (California) and medical director of the Fresno General Hospital.

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**Dr. Tomas Cervia,** Tenerife, Canary Islands, has recently been appointed Chief of Service, Department of Internal Medicine, Hospital Civil Insular and Medical Director of the Instituto de Fisiologia y Patologia Regional. Dr. Cervia is also medical director of the Sanatorio Antituberculoso Nacional de Ofra at Tenerife.

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**Dr. Edgar Mayer,** New York, New York, national chairman of the medical advisory board, National Jewish Hospital, Denver, Colorado, has been re-elected a trustee of the hospital.

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**Dr. Jay Arthur Myers,** Minneapolis, Minnesota, Past-President of the American College of Chest Physicians, was one of four distinguished alumni of the Ohio University, Athens, to be honored at the 150th Anniversary of the university. Dr. Myers was given the degree of LL.D. Congratulations!

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**Dr. Joseph E. Moody,** formerly of Ypsilanti, Michigan, has assumed directorship of the Boehne Tuberculosis Hospital, Evansville, Indiana. **Dr. Paul D. Crimm,** Sidney, Ohio, is the former medical director of the Boehne Hospital. Dr. Crimm has now entered private practice in Sidney.

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**Dr. Roger Hanna** has been named first director of state tuberculosis hospitals for Texas. Dr. Hanna was formerly superintendent and medical director of the Jackson County (Michigan) Tuberculosis Sanatorium.

**Dr. Herman E. Hilleboe,** Health Commissioner, New York State Department of Health, has been elected chairman of the New York State Joint Hospital Survey and Planning Commission.

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**Dr. Edward Dunner,** formerly of St. Louis, Missouri, has been appointed Chief of Training and Standards, Tuberculosis Service, Veterans Administration, Washington, D. C.

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**Dr. P. J. Sparer,** Memphis, Tennessee, has been appointed Assistant Professor of Psychiatry and Assistant Professor of Preventive Medicine at the University of Tennessee School of Medicine. Dr. Sparer was also elected Vice-President of the Tennessee Psychiatric Association and serves as Chairman of the Committee on Psychosomatic Aspects of Diseases of the Chest of the American College of Chest Physicians.

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**Dr. Nathaniel E. Reich,** Brooklyn, New York, Clinical Assistant Professor in Medicine, State University of New York College of Medicine, recently addressed the medical staff of the Boucicaut Hospital of the University of Paris (France) Medical School on "New Advances in the Treatment of Heart Diseases."

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**Dr. J. A. Stocker,** Springfield, Illinois and **Dr. W. J. Bryan,** Rockford, Illinois, were recently elected president and treasurer respectively of the Illinois Tuberculosis Association.

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## Council on Research

The Tobacco Industry Research Committee has notified the Council on Research of the American College of Chest Physicians that they are now in a position to consider applications for financial assistance for specific research projects dealing with the possible relationship of smoking to pulmonary disease and other diseases in the human. In order that an application may be considered by the Tobacco Industry Research Committee, it is necessary that it be accompanied by a complete outline of the project: its nature, its purpose and the method of execution, as well as an estimation of the financial assistance required.

If it is the wish of the applicant to have his project sponsored by the College, it will be necessary for him to submit it to the Council on Research of the College to be passed upon for approval before it is sent in to the Tobacco Industry Research Committee. Individual members can, of course, submit their applications directly to the Tobacco Industry Research Committee without having the approval of the Council on Research, but under such circumstances the projects would not be sponsored by the American College of Chest Physicians.

Application blanks can be obtained either directly from the office of the Tobacco Industry Research Committee or through Dr. Herman J. Moerch, the Chairman of the Council on Research of the American College of Chest Physicians.

Mr. Lionel H. Opie of the University of Cape Town, South Africa, receiving a check for $250 and a certificate from Dr. David P. Marais, Cape Town, Regent of the College for South Africa. Others pictured are members of the Southern Chapter of the College in South Africa. Mr. Arnold Victor (not pictured) of the State University of New York, U.S.A. tied for first prize and also received an award of $250 and a First Prize Certificate.

# 1955 Prize Essay Contest

The American College of Chest Physicians will offer three cash awards for the best essays written on any phase relating to the diagnosis and treatment of chest diseases (heart and/or lungs). First prize will be $250; Second prize, $100; and Third prize, $50. Each winner will also be awarded a certificate. The contest is open to undergraduate medical students throughout the world. The contest will close on April 10, 1955 and instructions for the preparation of manuscripts are as follows:

1) Five copies of the manuscript typewritten in English (double spaced) should be submitted to the Committee on College Essay, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

2) The only means of identification of the author shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside enclosing the name and address of the author.

3) A letter from the Dean or Chairman of the Department of Medicine or Surgery of the medical school certifying that the author is a medical student.

Members of the College are requested to bring this to the attention of undergraduate medical students.

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## ANNOUNCEMENTS

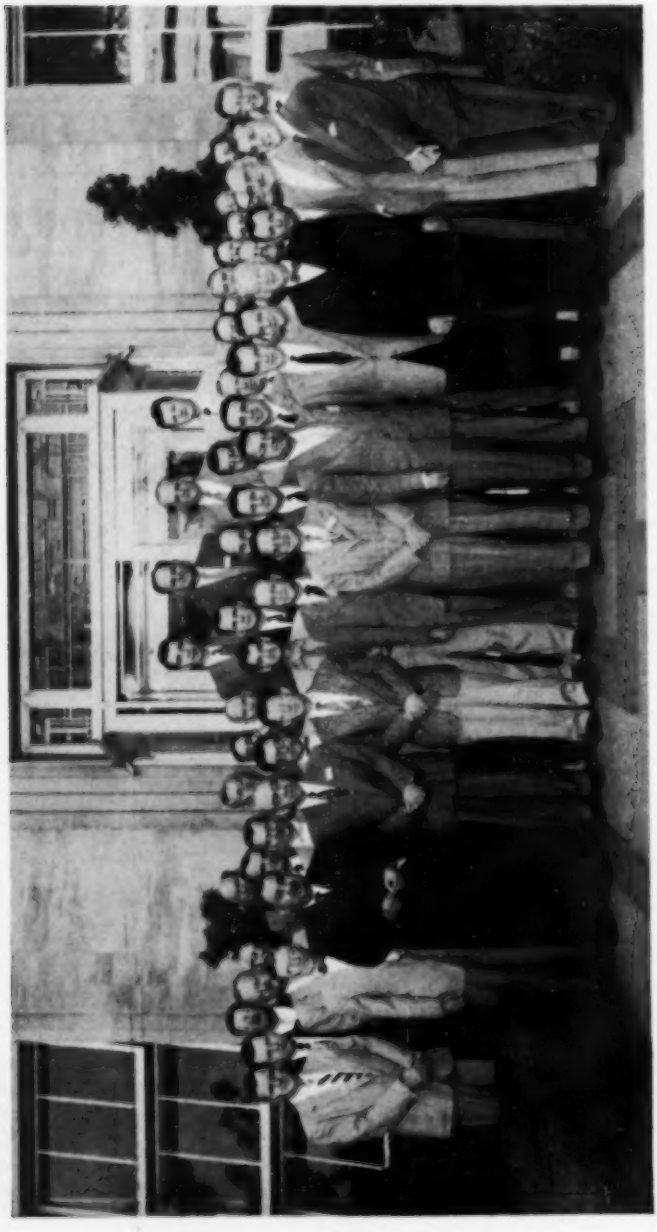
Six authorities on cancer will participate in the 1954 A. Walter Suiter Lecture, November 4, at the New York Academy of Medicine, in the form of a symposium entitled "Cancer: What We Know Today." Speakers will be Harold F. Dorn, Ph.D., Harold L. Stewart, Lauren V. Ackerman, Owen H. Wangensteen, Richard H. Chamberlain, and Alfred Gellhorn.

The Texas Medical Center at Houston, when facilities already under construction and on the drafting boards are completed, will comprise 3,350 beds, representing an outlay of more than $56 million on a 163 acre tract. Most of the funds for the development of the medical center have been raised by the people of Texas.

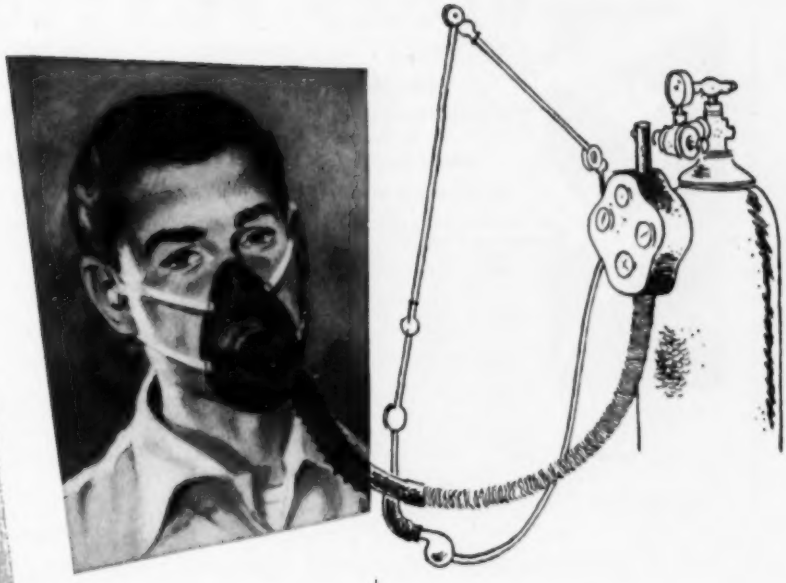
The University of Illinois College of Medicine has scheduled a Bronchoesophagology Course, under the direction of Dr. Paul H. Holinger, for the period November 8 through 20, 1954. Further information may be obtained by writing to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

The Bacteriology Laboratories of the Communicable Disease Center, Chamblee, Georgia, in cooperation with the Division of Special Health Services, Public Health Service, will offer a course in the laboratory diagnosis of tuberculosis, November 15-26, 1954. No tuition or laboratory fees are charged. Application forms may be obtained from Laboratory Training Services, Communicable Disease Center, Public Health Service, P. O. Box 185, Chamblee, Georgia.

The New York Medical College, Division of Graduate Studies and Department of Graduate Pediatrics, announces a Postgraduate Course in Pediatric Allergy under the Direction of Dr. Bret Ratner, Professor of Clinical Pediatrics and Associate Professor of Immunology. The course will include 30 sessions held on Wednesdays commencing November 3, 1954 through May 25, 1955. The tuition fee is $300. Applicants must be certified in pediatrics or have the requirements for certification. Apply to the Office of the Dean, New York Medical College, Fifth Avenue at 106th Street, New York 29, New York.



Participants in New Orleans Postgraduate Course on Diseases of the Chest, February 15-19, 1954.



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### Positions Available

Tuberculosis physicians wanted for New Mexico state sanatoria; under 50 years of age. Salary $6,000 to $10,000 plus living quarters. License in any state acceptable. For further information, please write to Department of Public Welfare, Santa Fe, New Mexico.

Medical Directorship, Firland Sanatorium, King County (Seattle) tuberculosis hospital. 750 beds. Excellent staff and facilities. Affiliation University of Washington. Apply to James W. Mifflin, Seaboard Building, Seattle, Washington.

The Veterans Administration Hospital, Kerrville, Texas, a 449 bed tuberculosis hospital, has vacancies for a chest physician (general practitioners eligible) and a pathologist. Starting salaries up to $10,800; positions based on the applicant's education and experience. Approved by American College of Surgeons and American Hospital Association. Affiliated with diplomate consultants in the various specialties who make regular visits. In the hills of Southwest Texas, only 65 miles from San Antonio on paved highway. Aliens with state license may be eligible for contract type appointment. Contact the Manager, VA Hospital, Kerrville, Texas.

## CALENDAR OF EVENTS

### NATIONAL MEETINGS

**Interim Session, American College of Chest Physicians Delano Hotel, Miami Beach, Florida, November 28-29, 1954**

**21st Annual Meeting, American College of Chest Physicians Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1955**

### POSTGRADUATE COURSES

9th Annual Postgraduate Course on Diseases of the Chest
Knickerbocker Hotel, Chicago, Illinois, October 18-22, 1954

Postgraduate Course on Diseases of the Chest
Bunts Institute, Cleveland, Ohio, October 27-28, 1954

7th Annual Postgraduate Course on Diseases of the Chest
Hotel New Yorker, New York City, November 8-12, 1954

8th Annual Postgraduate Course on Diseases of the Chest
Bellevue-Stratford Hotel, Philadelphia, Pennsylvania, Spring, 1955

### CHAPTER MEETINGS

North Carolina Chapter, Winston-Salem, October 16, 1954

Illinois Chapter, Chicago, October 21, 1954

Indiana Chapter, Indianapolis, October 26, 1954

Potomac and Virginia Chapters (Joint Meeting)
Washington, D. C. October 31, 1954

Southern Chapter, St. Louis, Missouri, November 8-11, 1954

Pacific Northwest Chapter, Portland, Oregon, November 12-13, 1954

Cuban Chapter, Havana, December 1, 1954

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